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ANNUAL PROGRESS REPORT

FY-91

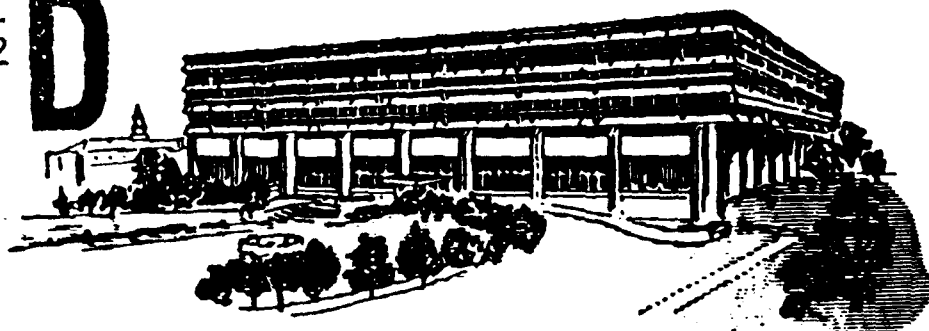


VOLUME I

pp 1-145



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DEPARTMENT OF CLINICAL INVESTIGATION
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5001

CLINICAL INVESTIGATION PROGRAM
RCS MED-300(RI)

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13. ABSTRACT (Maximum 200 words) This report identifies approved clinical research activities conducted at Walter Reed Army Medical Center through protocols approved by the Clinical Investigation Committee, the Human Use Committee/Institutional Review Board, and/or the Animal Use Committee, as appropriate. This report includes a Detail Summary Sheet outlining the progress of each protocol during Fiscal Year 91. Also included is a list of all known presentations and publications related to approved studies. All research was conducted under the provisions of AR 40-38 (Clinical Investigation Program, AR 40-7 (Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances, AR 70-25 (Use of Volunteers as Subjects of Research), HSC Reg 40-23 (Management of Clinical Investigations, Protocols, and Reports), and AR 70-18 (The Use of Animals in DOD Programs).				
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FORWARD

The Annual Progress Report (APR) documents the continuing review during FY-91 of research approved by the Clinical Investigation Committee (CIC), the Animal Use Committee (AUC), and the Human Use Committee/Institutional Review Board (HUC/IRB) of Walter Reed Army Medical Center (WRAMC). The review of each research protocol is initiated by the Department of Clinical Investigation (DCI) on the anniversary month of its approval. At that time, a request is sent to the principal investigator for submission of a progress report. The completed report consists of a detail summary sheet (DSS), an updated consent form, if needed, and a questionnaire regarding the continuing review of human subject participation or animal use. Members of the HUC/IRB or AUC review the progress reports throughout the year, and one of the following recommendations is made: 1) approval, 2) request additional information, or 3) request termination of the protocol. The members' recommendations are presented monthly to the HUC/IRB or AUC for final approval. The approved detail summary sheets of 551 protocols are included in this document.

The FY-91 APR process at WRAMC was administered by the Editorial Office, Research Administration Service, Department of Clinical Investigation, in coordination with the Research Review Service.



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I . UNIT SUMMARY

A. OBJECTIVE

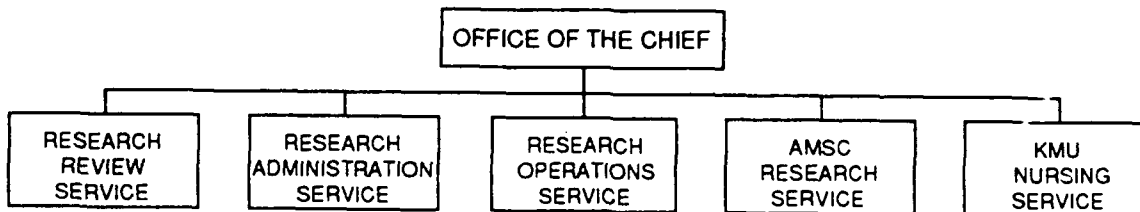
To implement and manage the clinical investigation program at Walter Reed Army Medical Center (WRAMC) by promoting, supporting, coordinating, planning, conducting, and publishing ethical, scientific inquiry into clinical health problems of beneficiaries of the military health care system, to include studies in humans and animals.

B. TECHNICAL APPROACH

The clinical investigation program at WRAMC is conducted in accordance with the following:

AR 40-7	Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances
AR 40-38	Clinical Investigation Program
AR 70-18	The Use of Animals in DOD Programs
TB MED 525	Control of Hazards to Health from Ionizing Radiation Used by the Army Medical Department
HSC 40-23	Management of Clinical Investigation Protocols and Reports
WRAMC 70-1	Clinical Investigation Program, WRAMC Research Activities
45 CFR 46	Protection of Human Subjects
21 CFR A,D,& F	Food and Drug Administration

C. ORGANIZATION SCHEME



D. DCI STAFF (Positions as of 30 September 1991)

DESCRIPTION	GRADE	MOS	BRANCH	NAME	ACTIVITY
<u>OFFICE OF THE CHIEF</u>					
Chief	06	61C	MC	Wray, HL	DCI
Secretary	07	0318	GS	Brock, ME	DCI
Medical Officer	15	0602	GM	Popovic, NA	Ortho Rsch
<u>RESEARCH REVIEW SERVICE</u>					
Chief	05	60F	MC	Derderian, SS	DCI
Biostatistician	13	1530	GS	Chang, AS	DCI
Statistician	12	1530	GS	Howard, RS	DCI
Computer Programmer	11	0334	GS	Rose, JG	DCI
Research Coordinator	09	1087	GS	Coleman-Fraser, E	DCI
Editorial Asst	05	1087	GS	Green, IL	DCI
Computer Room Supv	E5	01H10	SP	Gomez, RJ	DCI
<u>RESEARCH ADMINISTRATION SERVICE</u>					
Chief	12	0501	GS	Burton, ME	DCI
Tech Pub Editor	09	1083	GS	Kinsey, JM	DCI
Editorial Asst	07	1087	GS	Franklin, AD	DCI
Editorial Asst	07	1087	GS	Stacy, PG	DCI
Editorial Asst	06/07	1087	GS	Muchui, MJ	DCI
Supply Technician	06	2005	GS	Thomas, DR	DCI
Clerk Typist	04	0303	GS	Carter, C	DCI

DESCRIPTION	GRADE	MOS	BRANCH	NAME	ACTIVITY
(Research Administration Service cont.)					
Nurse Specialist	12	0610	GS	Abt, MB	Urology
Nurse Specialist	11	0610	GS	Asplund, L	Ortho Resch

Grant Personnel

Nurse Specialist	12	0610	GS	Myers, DV	Urology
Clinical Nurse	12	0610	GS	Jamison, J	Hem/Onc
Secretary	05	0318	GS	Bryson, DD	Hem/Onc
Clerk Med Typ	05	0318	GS	Sandfer, P	Pediatrics
Gen Health Sci	12	0601	GS	Summers, WV	AA&SC
Clinical Nurse	11	0610	GS	Vacant	Surg Resch
Dietitian	13	0630	GS	Mateski, DJ	Polyp Prev
Dietitian	11	0630	GS	Greaser, AM	Polyp Prev
Dietitian	11	0630	GS	Hancock, S	Polyp Prev
Dietitian	11	0630	GS	Miskovski, VJ	Polyp Prev

ARMY MEDICAL SPECIALIST CORPS CLINICAL INVESTIGATION AND RESEARCH SERVICE

Chief	05	65B9A	SP	Sweeney, JK	DCI
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RESEARCH OPERATIONS SERVICE

Chief	05	68F	MS	Lippert, LL	DCI
Med Lab NCO	E7	92B40	NC	Sheldon, GM	DCI
Bio Lab Tech	11	0404	GS	Kapur, JJ	DCI

DESCRIPTION	GRADE	MOS	BRANCH	NAME	ACTIVITY
<u>General Support Lab</u>					
Chief	03	68C00	MS	Payne, AM	DCI
Chemist	11	1320	GS	Abdel-Rahim, M	Biochem
Bio Lab NCO	E6	01H30	NC	Williams, C	DCI
Bio Sci Asst	E4	01H10	AMEDD	Vacant	Surg Resch
Med Lab Spec	E4	92B20	NC	Curtner, D	Cell Biology

<u>Animal Support Lab Research</u>					
Bio Lab Tech	10	0404	GS	Bailey, LR	Animal Resch

<u>Infectious Disease Research Laboratory</u>					
Microbiologist	12	0403	GS	Dobek, AS	DCI

<u>Transplant Immunology Laboratory</u>					
Med Lab NCO	E6	92B30	NC	Sullivan, S	DCI

<u>Kyle Metabolic Research Laboratory</u>					
C, Nutrition Care	03	65C00	SP	Coffey, L	DCI
Supv Resch Chem	14	1320	GS	Carr, FE	DCI
Physiologist	12	0413	GS	Lukes, YD	DCI
Chemist	12	1320	GS	Nicholson, DE	DCI
Chemist	11	1320	GS	Lahiri, S	DCI
Bio Lab Tech	09	0404	GS	Jenkins, EL	DCI
Med Tech	11	0644	GS	Barnes, SG	DCI

DESCRIPTION	GRADE	MOS	BRANCH	NAME	ACTIVITY
(Kyle Metabolic Research Laboratory cont.)					
Med Tech	05	0645	GS	Martin, JL	DCI
Editorial Asst	07	1087	GS	Jacobson, A	DCI
Secretary	05	0318	GS	Vacant	DCI
Med Lab NCO	E6	92B30	NC	Ansley, R	DCI
Chemist	12	1320	GS	Tseng, YC	DCI
Resch Asst	12	0610	GS	Solomon, BL	DCI
Med Tech	11	0644	GS	Anderson, JS	DCI
Med Lab Spec	E4	92B10	NC	Vacant	DCI

Lab Support Unit

Resch Chemist	12	0644	GS	Salata, KF	Allergy
Chemist	11	1320	GS	Maydonovich, CL	GI
Med Tech	11	0644	GS	Armstrong, JM	Rheum
Med Tech	11	0644	GS	Burgess, D	Pediatrics
Bio Sci NCO	E5	1H20	NC	Andrada, F	Pulmonary
Med Lab Spec	E7	1H20	NC	Guzman, J	Pulmonary
Med Tech	11	0644	GS	Berger, TA	Allergy
Microbiologist	12	0403	GS	Billups, L	Flow Cytom
Chemist	12	1320	GS	Vacant	Pulmonary

Kyle Metabolic Unit Nursing Service

Supv Clin Nurse	12	0610	GS	Parchment, VA	DCI
Clinical Nurse	11	0610	GS	Bicknell, E	DCI

DESCRIPTION	GRADE	MOS	BRANCH	NAME	ACTIVITY
(Kyle Metabolic Unit Nursing Service cont.)					
Clinical Nurse	11	0610	GS	Anderson, L	DCI
Clinical Nurse	10	0610	GS	Burman, MS	DCI
Clinical Nurse	11	0610	GS	Coleman, A	DCI
Clinical Nurse	11	0610	GS	Chaudhari, NP	DCI
Nurse Asst	05	0620	GS	Keeve, ML	DCI
Clinical Nurse	11	0610	GS	Saxon, NJ	DCI
Clinical Nurse	10	0610	GS	Stewart, MO	DCI
Clinical Nurse	11	0610	GS	Battle, OM	DCI
Clinical Nurse	9/11	0610	GS	Vacant	DCI
Clinical Nurse	9/11	0610	GS	Vacant	DCI

The Department increased its number of assigned personnel during this year to a record of 70. The Orthopaedic Surgery Service, Department of Surgery, expanded their Residency Training Program to include a fifth year dedicated primarily to conducting research. Dr. Neven Popovic was hired to coordinate and oversee orthopaedic research, which includes a nurse specialist as Research Coordinator. LTC James Kikendall, MC, Gastroenterology Service, Department of Medicine, was awarded a National Institutes of Health (NIH) grant to conduct a 7-year polyp prevention study that will look at dietary intervention. A Research Coordinator, Ms. Donna Mateski, M.S., was hired to oversee the project and staff, of which three have been hired. During the past fiscal year, the Kyle Metabolic Unit Nursing Service relocated to the 7th floor of the hospital and increased its assigned staff, significantly decreasing its reliance on agency contract nurses.

E. DCI FINANCIAL SUPPORT

	FY-87	FY-88	FY-89	FY-90	FY-91
Civilian Personnel	\$ 947,549	\$1,000,206	\$1,000,402	\$1,500,001	\$1,922,896
Consumable Supplies	\$ 652,020	\$ 708,411	\$ 707,272	\$ 708,572	\$ 650,531
Civilian Contracts	\$ 121,579	\$ 115,000	\$ 88,898	\$ 107,000	\$ 204,385
TDY	\$ 23,182	\$ 28,401	\$ 35,186	\$ 36,102	\$ 31,399
Capital Expense Equipment Program	\$ 38,734	\$ 32,000	\$ 57,860	\$ 30,932	\$ 77,164
MEDCASE	\$ 945,657	\$ 694,078	\$ 557,178	\$ 572,892	\$1,000,076
Other Grants	\$ 532,560	\$ 254,102	\$ 298,467	\$ 528,140	\$ 500,252
Military	\$ 831,253*	\$ 432,504	\$ 429,718	\$ 392,137	\$ 397,960
T O T A L	\$4,092,534	\$3,264,702	\$3,174,981	\$3,875,776	\$4,784,664

*Includes benefits

F. RESEARCH ACTIVITY

1. Accomplished in FY-91

With the mission to empower WRAMC researchers from planning to publication, the Department of Clinical Investigation (DCI) supported a record total of 705 active protocols this year (Table I). Twenty-two percent (154) of these studies were newly approved during the fiscal year, leaving 551 ongoing for at least one year that are summarized in this report. Medical Corps officers at WRAMC were Principal Investigators of 87% of the investigations. Medical Corps activities account for 95% of the investigations, and about 1% were conducted at Army Community Hospitals in the Walter Reed Health Service Region (Table II). Human studies accounted for 93% of the investigations, with 29% involving research therapies including investigational drugs or devices and cooperative oncology group studies (Table III). Animal studies accounted for 6%, and laboratory studies accounted for 1%. Clinical investigation productivity by WRAMC researchers included 75 published abstracts, 71 published articles, and 110 conference presentations (Table IV). There were 31 Clinical Investigation Recognition Seminars (now in its fifth year) presented by WRAMC researchers, providing local dissemination of WRAMC research presented at regional and national conferences.

TABLE I. WRAMC Protocol Activity

PROTOCOLS	FY-86	FY-87	FY-88	FY-89	FY-90	FY-91
ONGOING at the begining of FY	383	408	456	474	520	551
NEWLY APPROVED (+)	159	170	145	197	172	153
TOTAL ACTIVE During FY	542	578	601	671	692	704
COMPLETED (-)	123	78	114	118	129	164
TERMINATED (-)	11	44	13	33	12	6
ONGOING at the end of FY	408	456	474	520	551	534

TABLE II. WRAMC FY-91 Active Investigations by AMEDD Officer Corps

CORPS	GRAD TX PROG # (%)	OFFICERS IN TX # (%)	ACTIVE STUDIES # (%)
Medical	53 (80)	429 (89)	665 (95)
Medical Service	9 (14)	31 (7)	13 (2)
Medical Specialist	2 (3)	11 (2)	8 (1)
Dental	2 (3)	9 (2)	2 (<1)
Nursing	0 (0)	0 (0)	10 (1)
Veterinary	0 (0)	0 (0)	1 (<1)
	66 (100)	480 (100)	699 (100)
Army Community Hospitals			5

TABLE III WRAMC FY-91 Active Investigations by Subject

SUBJECT	ACTIVE STUDIES	
	#	(%)
Human	658	(93)
Invest New Drug	44	(6)
Invest Device	7	(1)
Cooperative Oncology Group	155	(22)
Descriptive - Expedited	155	(22)
Greater Risk	<u>297</u>	<u>(42)</u>
	658	(93)
Animal	45	(6)
Laboratory	1	(<1)
	<u>704</u>	<u>(100)</u>

TABLE IV. WRAMC Clinical Investigation Publications and Presentations

	FY-86	FY-87	FY-88	FY-89*	FY-90**	FY-91**
Published Articles	79	55	104	22	62	71
Abstracts	119	86	106	73	67	75
Presentations	75	55	93	61	106	110

* Based on data from approved clinical investigations.

+ WRAMC reported a total of 270 publications for CY89 and 427 publications for CY90 in a bibliography produced by the staff of the Medical Library. Journal articles, books, book chapters, and letters indexed by MEDLINE were included.

The DCI Quality Improvement Questionnaire was an anonymous survey conducted in June 1991. Every Principal Investigator and Service Chief received one questionnaire, regardless of the number of active protocols each held individually. Department and Service Chiefs were included even if they were not principal investigators.

There were 127 responses received from the 283 questionnaires sent, as follows:

	<u># Sent</u>	<u># Returned</u>	<u># Comments</u>
Department Chiefs	19	11 (58%)	5 (46%)
Service Chiefs	51	22 (43%)	8 (36%)
Investigators	213	94 (44%)	38 (40%)
TOTAL	283	127 (45%)	51 (40%)

The following 12 questions were presented, with questions 1 and 10 revised for the 1991 survey:

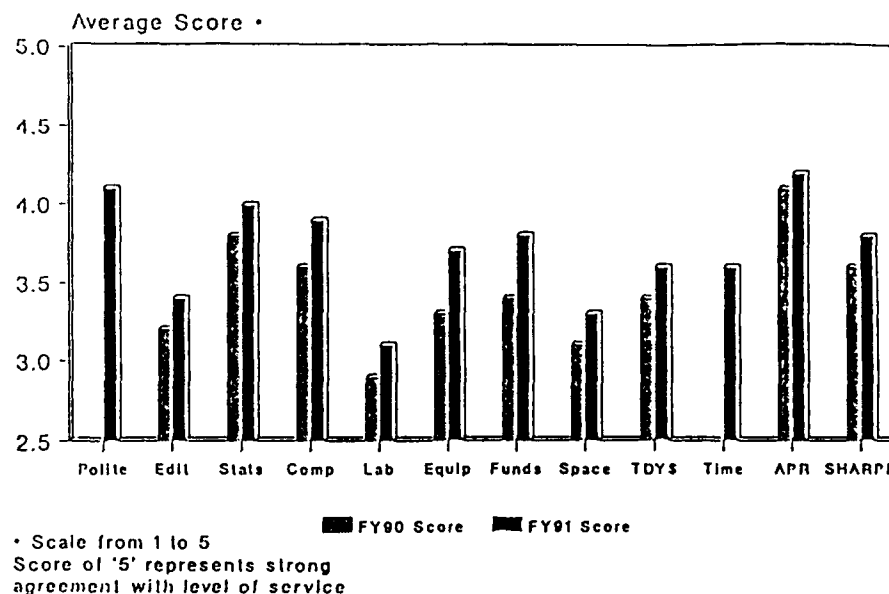
1. DCI is courteous and professional when interacting with researchers on the telephone and in person.
2. DCI is providing adequate editorial and clerical support in preparing protocols.
3. DCI is providing adequate statistical consultation.
4. DCI is making available adequate computer support.
5. DCI is providing adequate laboratory technician support.
6. DCI is providing adequate equipment support.
7. DCI is providing adequate funding for supplies and contract services.
8. DCI is providing adequate laboratory research space.
9. DCI is providing adequate financial support for paper presentation TDY.
10. DCI/WRAMC's review process approves protocols in a timely manner.
11. DCI conducts an adequate annual review of research protocols.
12. Overall, DCI lives up to its slogan of being SHARPP: Striving to Help All Researchers from Planning to Publication.

The choice of answers ranged from "Strongly Agree" (score = 5) to "Strongly Disagree" (score = 1), with an option of "Not Applicable."

As reflected by the following chart, the Annual Progress Report (APR), courteous and professional demeanor of staff members, and statistical consultation were the top three total average scores. Equipment support,

funding for supplies and services, and computer support had the three largest improvements in ratings compared with FY90. Compared to the 1990 survey, the total mean score increased from 3.49 to 3.81 in 1991. For the 10 questions that were unchanged, the mean scores improved in each case.

Evaluation of Performance FY90-91 By Type of Service



Editorial and clerical support for protocol preparation and the protocol approval time have improved, but these areas should have major improvements during FY92 now that staffing shortages have been resolved. Laboratory space and technical support have improved, but continued intense attention is required toward enhancing the utilization and productivity for the short-term. The strategic planning process should help in these areas for the long-term.

Operation Desert Shield and Storm required that WRAMC prepare to be the major combat casualty receiving center and caused significant upheaval among the professional staff. Its impact on the clinical investigation program was most apparent in the decreased number of protocols approved during FY91: 154, down from 172 in FY90.

The Department of Clinical Investigation strategic plan was approved in August 1991. The Base Realignment and Closure (BRAC) transition will require additional missions at WRAMC, with plans including the construction of a new clinic building in which the DCI administrative offices will be located on the fourth floor in FY94.

The first Medical Corps training program in Clinical Investigation was initiated at WRAMC in July 1991.

The prestigious Bailey K. Ashford Clinical Research Award is bestowed annually on a member of the year's graduating class whose research accomplishments excelled during training. Nineteen graduating trainees, representing 16 training programs, were nominated for the 1991 award. From the nominees, five finalists are selected to present the results of their research at a symposium sponsored by the Department of Clinical Investigation. The 1991 finalists were: MAJ Henry B. Burch, MC, Fellow, Endocrine-Metabolic Service, Department of Medicine, "Immunogenicity of a unique region of the human thyrotropin receptor"; MAJ R. David Heekin, MC, Senior Resident, Orthopaedic Surgery Service, Department of Surgery, "A comprehensive analysis of primary porous coated anatomic (PCA) total hip arthroplasty"; CPT Christian F. Ockenhouse, MC, Senior Resident, Internal Medicine Service, Department of Medicine, "Molecular design of endothelial receptor analogues for severe and complicated malaria therapy"; MAJ David W. Polly, Jr., MC, Senior Resident, Orthopaedic Surgery Service, Department of Surgery, "The efficacy of biodegradable microencapsulated antibiotics for preventing infection in an open fracture, internal fixation model"; and MAJ Gary R. Simonds, Chief Resident, Neurosurgery Service, Department of Surgery, "Experimental neural transplantation in the rat Parkinson's model: Effects of intraventricular substantia nigra allografts as a function of donor age." Recipient of the 1991 Bailey K. Ashford Clinical Research Award, CPT Christian F. Ockenhouse, was announced at graduation in June.

The Research Review Service hired Mrs. Estelle Coleman-Fraser as the Research Review Coordinator, filling a critical vacancy in the Department. The Biostatistical and Computer Support Section expanded educational programs directed at training researchers in the use of statistics in medical research by presenting a two-day seminar on research design and statistical methods.

The Research Administration Service continued to grow in both workload and staff. Supporting the Department and all WRAMC investigators, this Service managed intra- and extramural monies totalling over \$4,500,000. Of this total, over \$1,000,000 was received by the Department in MEDCASE funds. Extramural funding continued to expand and includes support from the National Institutes of Health and the U.S. Army Medical Research and Development Command, as well as gifts and grants. In August 1991, an Assistant Administrator was assigned to provide additional support and management. Additionally, four new employees joined the staff in support positions; a Clerk-Typist and three Editorial Assistants. The growth in the Editorial Office has allowed further extension of services to WRAMC investigators in the preparation of research protocols, as well as abstracts and manuscripts for publication. One of the Editorial Assistants has been assigned responsibility for the compilation of the WRAMC Annual Progress Report, which reports the progress of each research study ongoing at WRAMC (FY-91 total = 551). Additionally, the Editorial Office began writing and publishing an informative bi-monthly newsletter for all WRAMC investigators.

During 1991, the Research Operations Service significantly expanded, refined, and upgraded laboratory activities. Ophthalmology, Nephrology, and Rheumatology Services established or greatly expanded their research laboratories. The DCI Animal Facility was upgraded through the installation of a clean room for survival surgeries and the procurement of an intensive

care unit, bedding dump station, and additional operating room equipment. Funding also became available for purchase and installation of a cage washing system. Computer automation was greatly enhanced in the Biochemistry laboratory. Hardware and software were purchased and applications established for instrument control, data acquisition and analysis, hazardous chemical inventory and tracking, and hazardous waste reporting.

In April 1991, the Kyle Metabolic Unit Nursing Service came under the leadership of its new head nurse, Ms. Verna Parchment, and in August 1991, moved from Ward 47 to Ward 75. The Kyle Metabolic Unit research laboratories continued hosting Dr. Endre Nagy, M.D., as a foreign trainee from Budapest, Hungary, in his Fogarty Fellowship.

Surgical research received continuing emphasis with LTC Charles J. Yowler, MC, assuming the duties of Chief of Surgical Research, replacing COL Samuel A. Cucinell, MC, who served from July 1989 to June 1991. Dr. Neven A. Popovic, M.D., Ph.D., was recruited to the new position of Director of Orthopaedic Research.

Principal Investigators conducting research under the Clinical Investigation Program at WRAMC received several recognitions during 1991 for their outstanding research. The specific awards and awardees were:

LTC Thomas Wiswell, MC, USA, Department of Pediatrics, was a finalist for the Andrew Margileth Research Award for 1991, presented by the Uniformed Services Section of the Academy of Pediatrics. His paper, entitled "Staphylococcus aureus colonization following neonatal circumcision: Is there device dependency?", was subsequently published in the Journal of Pediatrics 1991;119:302-4.

LTC Darrel C. Bjornson, MS, USA, Pharmacy Service, was awarded the Pharmacy Research Award in recognition of his excellence in research. The award is sponsored by Army Pharmacy and was presented at the Ralph D. Arnold Pharmaceutical Services Course, San Antonio, TX, in September 1991. Both Dr. Bjornson's past distinguished research activities, as well as his present work in both the HIV research arena and the evaluation of clinical pharmacy services, were cited.

2. Planned for FY-92

After a difficult year because of the Gulf War, DCI hopes to work closely with the professional staff to improve all aspects of the WRAMC Clinical Investigation Program. Activities which were not fully completed in FY-91 will be undertaken in FY-92, and include:

(a) Continued expansion of the Editorial Office to more fully meet the needs of the medical center for preparation of research applications, presentations, and manuscripts.

(b) Implementation of the Interagency Support Agreement between WRAIR and WRAMC to provide more effective audiovisual support for research illustrations and poster presentations.

(c) Solicitation of potential contributors to the WRAMC Clinical Investigation Special Project Fund (through the Jackson Foundation).

(d) Enhancement of the DCI local area network (DCINET) to increase use by the clinical investigators, as well as the administrative staff of the Department. This should facilitate use of the statistical and data analysis capabilities and the graphics support available.

(e) Solidification of the plans to renovate the animal facility to meet AAALAC accreditation requirements.

New activities planned for the upcoming fiscal year include:

(a) Development of a center-wide research course to be given in the Fall of 1992. This course will be directed to personnel in training and is our first effort at providing an introductory program on research methods and to introduce the services and facilities available to WRAMC investigators.

(b) Completion of milestones outlined in the Department's strategic plan; i.e., submission of a Schedule X for proposed manpower requirements and development of enhanced 5-year plans for both MEDCASE and CEEP programs.

3. Ongoing and Future Issues

The downsizing of the Army and the institution of the DOD Coordinated Care Program will require careful planning by the Department of Clinical Investigation in order to flourish in this new environment.

Funding of the Clinical Investigation Program appears to be a crucial issue. The need for an Army-wide mechanism to resource the Clinical Investigation Programs is essential. Extramural funding will have to be expanded beyond the Henry M. Jackson Foundation for the Advancement of Military Medicine and the U.S. Army Medical Research and Development Command.

Ongoing as a major issue at WRAMC is the time required to obtain approval for research projects. DCI places the highest priority on this issue and tracks each protocol to ensure its ultimate approval.

TABLE V: Human Use Committee/Institutional Review Board Members

Thomas A. Klein, COL MC	Chairman Chief, Dept of Obstetrics & Gynecology Representing Deputy Commander
H. Linton Wray, COL MC	Co-Chairman Chief, Dept of Clinical Investigation
Valerie Biskey, COL AN	Chief, Nursing Research Representing Chief, Dept of Nursing
Darrel Bjornson, LTC MS	OIC, Hematology-Oncology Pharmacy Representing Chief, Pharmacy Service
Sarkis Derderian, LTC MC	Assistant Chief, DCI
Jack Farrell, Ph.D.*+	Chief, Psychology Section U.S. Soldiers' & Airmens' Home
James Herndon, MAJ CH	Chaplain Representing Ch, Dept of Ministry and Pastoral Care
Eric Marks, M.D.*	Associate Professor Dept of Medicine, USUHS
Laurel Meaney, DAC	Patients' Rights Representative, WRAMC
Scott Murdoch, J.D.	Chief, Claims Office Representing Center Judge Advocate
Richard Patterson, LTC SP	Chief, Education and Research Nutrition Care Directorate Representing Ch, Nutrition Care Dir
Robert Smallridge, COL MC*	Chief, Dept of Clinical Physiology Division of Medicine, WRAIR Representing Director, WRAIR

*Non-affiliated

TABLE VI: Clinical Investigation Committee Members

Sarkis Derderian, LTC MC	Acting Chairman Assistant Chief, DCI
Stephen Sihelnik, LTC MC	Acting Co-Chairman Staff, Urology Service, Dept of Surgery
Jay Anderson, COL MC	Chief, Nuclear Medicine Representing Radiation Control Comm
Audrey Chang, Ph.D.	Senior Biostatistician, DCI
Samuel Cucinell, COL MC	Chief, Surgical Research Representing Chief, Dept of Surgery
Gary Klipple, COL MC	Chief, Rheumatology Service Representing Chief, Dept of Medicine
Scott Murdoch, J.D.	Chief, Claims Office Representing Center Judge Advocate
Jean Reeder, LTC AN	Nursing Research Representing Ch, Nursing Research Svc
Jane Sweeney, COL SP	Chief, AMSC Research

TABLE VII: Rotating Senior Investigators, Clinical Investigation Committee

Brian Walden, Ph.D.	Army Audiology & Speech Center
Bahman Jabbari, COL MC	Neurology Service
Terry Schultz, COL MC	Department of Psychiatry
Steven Shay, COL MC	Gastroenterology Service
Gary Carpenter, COL MC	Allergy-Immunology Service
Thomas Wiswell, LTC MC	Department of Pediatrics

**TABLE VIII: Animal Use Committee/Clinical Investigation
Committee Members**

Charles Raflo, COL VC	Attending Veterinarian Chief, Animal Resource Department, Div of Veterinary Medicine, WRAIR
Lloyd Lippert, LTC MS	Ch, Research Operations Service Dept of Clinical Investigation, WRAMC
Hernando Mena, LTC MC*	Asst Chairman, Dept of Neuropathology Armed Forces Institute of Pathology
Ted Hadfield, MAJ BSC*	Armed Forces Institute of Pathology

*Non-affiliated

TABLE IX: HIV Research/Clinical Investigation Committee Members

Charles Oster, COL MC	Chief, Infectious Disease Service Representing Program Director, HIV Research, Jackson Foundation
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EXPENSES FOR PROTOCOLS OF CURRENT AND PREVIOUS FISCAL YEARS,
BY DEPARTMENT AND SERVICE, LISTED IN ALPHABETICAL ORDER

DEPARTMENT/ SERVICE	PROTOCOL NUMBER*	PRIOR FY's (\$)	CURRENT FY (\$)	TOTAL (\$)
ALLERGY-IMMUNOLOGY SERVICE				
	3221	21,527	0	21,527
	3339	0	3,794	3,794
	3340	7,478	0	7,478
	3343	7,354	20	7,374
	3344	5	0	5
	3345	330	0	330
	3346	1,462	79	1,541
	3347	40	0	40
	3349	0	2,763	2,763
	3350	0	40	40
	3351	0	271	271
	3352	0	1,439	1,439
	3353	0	530	530
	3354	0	3,344	3,344
	3355	0	205	205
	3357	0	3,533	3,533
	3358	0	2,097	2,097
	TOTAL	38,196	18,115	56,311
DEPARTMENT OF CLINICAL INVESTIGATION				
	2584	2,858	0	2,858
	9263	1,446	0	1,446
	9268	5,881	683	6,564
	9271	12,446	695	13,141
	9272	33,643	1,802	35,445
	9275	16,417	374	16,791
	9276	8,841	0	8,841
	9278	8,526	4,199	12,725
	9280	0	2,535	2,535
	9281	0	2,253	2,253
	TOTAL	90,058	12,541	102,599
HIV RESEARCH				
	8802	0	996	996
	TOTAL	0	996	996
DEPARTMENT OF MEDICINE				
Dermatology Service				
	1805	217,394	0	217,394
	TOTAL	217,394	0	217,394
DEPARTMENT OF MEDICINE				
Endocrine-Metabolic Service				
	1300-88	2,400	355	2,755
	1302-88	15,348	28	15,376
	1308-88	1,520	0	1,520
	1309-88	11,846	3,430	15,276
	1310-88	10,649	0	10,649

* Protocol is not listed if total expense is zero.

EXPENSES FOR PROTOCOLS OF CURRENT AND PREVIOUS FISCAL YEARS,
BY DEPARTMENT AND SERVICE, LISTED IN ALPHABETICAL ORDER

DEPARTMENT/ SERVICE	PROTOCOL NUMBER*	PRIOR FY's (\$)	CURRENT FY (\$)	TOTAL (\$)
DEPARTMENT OF MEDICINE				
Endocrine-Metabolic Service (continued)				
	1312-89	737	0	737
	1313-89	10,521	825	11,346
	1315-89	560	0	560
	1316-89	5,006	0	5,006
	1320-90	0	3,304	3,304
	1321-90	0	12,689	12,689
	1322-90	0	427	427
	1349-84	18,471	903	19,374
	1351-84	538	0	538
	1356-84	4,352	0	4,352
	1359-85	49,718	410	50,128
	1361-85	80,475	0	80,475
	1363-85	13,475	1,096	14,571
	1367-86	7,181	0	7,181
	1369-86	4,353	0	4,353
	1371-86	6,958	3,747	10,705
	1372-86	61,131	3,124	64,255
	1376-86	18,811	0	18,811
	1384-86	4,234	0	4,234
	1385-87	60,808	1,748	62,556
	1386-87	3,979	0	3,979
	1387-87	29,853	9,151	39,004
	1389-87	0	13,020	13,020
	1390-87	37,429	44,476	81,905
	1391-87	814	0	814
	1393-87	128,378	14,125	142,503
	1394-87	20,867	0	20,867
	1395-87	86,470	58,199	144,669
	1399-87	51,686	38,812	90,498
	4299	0	13,443	13,443
	4300	0	9,013	9,013
	9266	21,688	2,275	23,963
	TOTAL	770,256	234,600	1,004,856
DEPARTMENT OF MEDICINE				
Gastroenterology Service				
	1400-88	2,658	0	2,658
	1401	1,865	4,014	5,879
	1403	415	0	415
	1404	50	50	100
	1406	4,931	3,142	8,073
	1409	1,100	207	1,307
	1411	0	1,510	1,510
	1413	0	34,319	34,319

* Protocol is not listed if total expense is zero.

EXPENSES FOR PROTOCOLS OF CURRENT AND PREVIOUS FISCAL YEARS,
BY DEPARTMENT AND SERVICE, LISTED IN ALPHABETICAL ORDER

DEPARTMENT/ SERVICE	PROTOCOL NUMBER*	PRIOR FY's (\$)	CURRENT FY (\$)	TOTAL (\$)
DEPARTMENT OF MEDICINE				
Gastroenterology Service (continued)				
	1414	0	27,722	27,722
	1416	0	1,484	1,484
	1417	0	3,602	3,602
	1435	239	0	239
	1450	13,484	0	13,484
	1453	49	0	49
	1462	2,921	220	3,141
	1470	1,567	0	1,567
	1471	1,549	160	1,709
	1483	2,329	11	2,340
	1487	1,158	0	1,158
	1489	450	878	1,328
	1493	390	0	390
	1495	2,975	1,185	4,160
	1496	525	0	525
	1497	1,250	0	1,250
	2031	602	0	602
	TOTAL	40,507	78,504	119,011
DEPARTMENT OF MEDICINE				
Hematology-Oncology Service				
	1616-82	2,144	0	2,144
	1639-86	0	445	445
	1657-88	13,650	0	13,650
	1673	0	5,469	5,469
	TOTAL	15,794	5,914	21,708
DEPARTMENT OF MEDICINE				
Infectious Disease Service				
	1956	7,236	0	7,236
	1971	0	4,308	4,308
	TOTAL	7,236	4,308	11,544
DEPARTMENT OF MEDICINE				
Nephrology Service				
	1152	1,332	0	1,332
	1156	1,131	0	1,131
	1157	7,796	0	7,796
	1158	1,463	0	1,463
	1160	17,513	218	17,731
	TOTAL	29,235	218	29,453
DEPARTMENT OF MEDICINE				
Pulmonary Disease Service				
	1707	6,976	4,291	11,267
	1711	157	0	157
	1714	220	0	220

* Protocol is not listed if total expense is zero.

EXPENSES FOR PROTOCOLS OF CURRENT AND PREVIOUS FISCAL YEARS,
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DEPARTMENT/ SERVICE	PROTOCOL NUMBER*	PRIOR FY's (\$)	CURRENT FY (\$)	TOTAL (\$)
DEPARTMENT OF MEDICINE				
Pulmonary Disease Service (continued)				
	1717	945	145	1,090
	1720	18,860	11,332	30,192
	1721	326	0	326
	1724	1,882	97	1,979
	1728	388	0	388
	1730	721	0	721
	1732	4,369	818	5,187
	1734	1,230	0	1,230
	TOTAL	36,074	16,683	52,757
DEPARTMENT OF MEDICINE				
Rheumatology Service				
	3220R	12,040	9,204	21,244
	3703	723	0	723
	3707	0	2,329	2,329
	TOTAL	12,763	11,533	24,296
NEUROLOGY SERVICE				
	7140	835	0	835
	7142	295	0	295
	9200	6,875	0	6,875
	TOTAL	8,005	0	8,005
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY				
	4243	50	0	50
	4279	0	908	908
	TOTAL	50	908	958
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY				
Gynecologic Oncology Group				
	4265	238	0	238
	TOTAL	238	0	238
DEPARTMENT OF PATHOLOGY AND AREA LABORATORIES				
	4807	0	6,821	6,821
	TOTAL	0	6,821	6,821
DEPARTMENT OF PEDIATRICS				
	6059	3,031	0	3,031
	6061	317	456	773
	6064	5,054	4,100	9,154
	6215	8,545	0	8,545
	6241	2,920	143	3,063
	6245	1,878	0	1,878
	6246	0	232	232
	6256	0	67	67
	6257	0	8,681	8,681
	6273	0	4,374	4,374
	TOTAL	21,745	18,053	39,798

* Protocol is not listed if total expense is zero.

EXPENSES FOR PROTOCOLS OF CURRENT AND PREVIOUS FISCAL YEARS,
BY DEPARTMENT AND SERVICE, LISTED IN ALPHABETICAL ORDER

DEPARTMENT/ SERVICE	PROTOCOL NUMBER*	PRIOR FY's (\$)	CURRENT FY (\$)	TOTAL (\$)
DEPARTMENT OF PEDIATRICS				
Pediatric Oncology Group				
	6213	8,241	3,720	11,961
	TOTAL	8,241	3,720	11,961
DEPARTMENT OF PSYCHIATRY				
	1326-90	0	34	34
	7242	0	5,496	5,496
	TOTAL	0	5,530	5,530
DEPARTMENT OF SURGERY				
Army Audiology and Speech Center				
	2504	0	1,119	1,119
	2505	0	168	168
	2506	0	466	466
	2574	1,176	0	1,176
	2577	5,849	9,453	15,302
	2588	992	2,913	3,905
	2590	4,355	650	5,005
	2591	2,099	40	2,139
	2593	5,988	0	5,988
	2594	3,329	2,891	6,220
	2596	2,449	1,862	4,311
	2598	0	1,995	1,995
	TOTAL	26,237	21,557	47,794
DEPARTMENT OF SURGERY				
Critical Care Medicine Service				
	3008	0	4,608	4,608
	TOTAL	0	4,608	4,608
DEPARTMENT OF SURGERY				
General Surgery Service				
	2037	1,365	0	1,365
	2048	0	15,076	15,076
	2049	0	1,590	1,590
	TOTAL	1,365	16,666	18,031
DEPARTMENT OF SURGERY				
Ophthalmology Service				
	2319	0	3,969	3,969
	TOTAL	0	3,969	3,969
DEPARTMENT OF SURGERY				
Organ Transplant Service				
	2630	362	0	362
	2631	2,195	0	2,195
	TOTAL	2,557	0	2,557

* Protocol is not listed if total expense is zero.

EXPENSES FOR PROTOCOLS OF CURRENT AND PREVIOUS FISCAL YEARS,
BY DEPARTMENT AND SERVICE, LISTED IN ALPHABETICAL ORDER

DEPARTMENT/ SERVICE	PROTOCOL NUMBER*	PRIOR FY's (\$)	CURRENT FY (\$)	TOTAL (\$)
DEPARTMENT OF SURGERY				
Orthopaedic Surgery Service				
	2404	75	0	75
	2410	8,439	0	8,439
	2411	0	1,206	1,206
	2412	1,707	0	1,707
	2413	2,910	0	2,910
	2414	196	0	196
	2422	0	1,238	1,238
	2423	0	797	797
	TOTAL	13,327	3,241	16,568
DEPARTMENT OF SURGERY				
Otolaryngology-Head & Neck Surgery Svc				
	2501	0	5,874	5,874
	TOTAL	0	5,874	5,874
DEPARTMENT OF SURGERY				
Plastic Surgery Service				
	2909	0	1,042	1,042
	TOTAL	0	1,042	1,042
DEPARTMENT OF SURGERY				
Urology Service				
	2862	0	5,109	5,109
	2864	0	500	500
	TOTAL	0	5,609	5,609
VETERINARY SERVICE				
	9801	66	232	298
	TOTAL	66	232	298

* Protocol is not listed if total expense is zero.

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3221	Engler, Renata MAJ MC. The Role of IgG Subclasses in Hymenoptera Hypersensitivity and Immunotherapy (8/84)	1
3336	Moyer, Joseph MAJ MC. The Effect of Human Breast Milk Cell Supernatants on In Vitro Immunoglobulin Secretion (11/87)	2
3339	Squire, Edward LTC MC. Comparison of House Dust Mite Educational Programs on Selected Outcome Variables (7/88)	3
3340	Salata, Kalman PhD. Analysis of Carbohydrate Epitopes on Food Allergen Proteins: A Pilot Study (8/88)	4
3341	Squire, Edward LTC MC. Occurrence of Laryngeal Dysfunction Among Patients Initially Diagnosed as Having Bronchial Asthma (8/88)	5
3343	Salata, Kalman PhD. Standardized Vs. Nonstandardized Allergen Products Containing Dust Mite Antigens (10/88)	6
3344	Carpenter, Gary COL MC. The Effect of UVB (Ultraviolet-B) Light on Immediate, Late and Delayed Hypersensitivity (12/88)	7
3345	Salata, Kalman PhD. Cross Allergenicity of Pollen Allergens from American Linden and European Linden (6/89)	8
3346	Salata, Kalman PhD. Comparison of Three Methods of Assessing Induction of Mitogen and Allergen Specific Lymphocyte Proliferation (6/89)	9
3347	Salata, Kalman PhD. A Simple Prick Puncture End Point Titration Procedure to Evaluate the Safety of Switching from Nonstandardized to Standardized Allergen Extracts for Use in Immunotherapy (8/89)	10
3348	Engler, Renata LTC MC. Immunotherapy Reactions (11/89)	11
3349	Salata, Kalman PhD. Mitogen-Inducible T Suppressor Cell Assay by Flow Cytometry (12/89)	12
3350	Salata, Kalman PhD. Flow Cytometric Analysis of Natural Killer Cell Activity and Antibody-Dependent Cell-Mediated Cytotoxicity (1/90)	13

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3351	Salata, Kalman PhD. In Vitro House Dust Mite Allergy Assays: Comparison of a Monoclonal Antibody/Allergen Capture Method with a Fluorescent Allergosorbant Test (1/90)	14
3352	Squire, Edward LTC MC. Use of Steroid Sparing Agents Among Asthmatics Doing Poorly on Corticosteroids: A Pilot Study (1/90)	15
3353	Salata, Kalman PhD. Contrasuppressor Cells in Allergy Immunotherapy (3/90)	16
3354	Salata, Kalman PhD. Two Way Mixed Lymphocyte Culture: Analysis by Two Color Flow Cytometry (4/90)	17
3355	Salata, Kalman PhD. Effect of Methotrexate on Expression of Intercellular Adhesion Molecule I in Interleukin-1 Stimulated Cultured Human Cells (5/90)	18
3356	Davis, William CPT MC. High Dose Intravenous Immunoglobulin in the Treatment of Chronic Inflammatory Demyelinating Polyneuropathy (8/90)	19
3357	Lieberman, Alan CPT MC. Serum and Secretory Immune Status of Patients with Chronic Sinusitis and Normals (9/90)	20
3358	Salata, Kalman PhD. Plasma Level of Mast Cell Tryptase in Patients Undergoing Immunodiagnostic or Immunotherapy Procedures who Experience Adverse Reactions (9/90)	21

DEPARTMENT OF CLINICAL INVESTIGATION

2584	Derderian, Sarkis LTC MC. Evaluation of Patients with Obstructive Sleep Apnea Syndrome Following Uvulopalatopharyngoplasty (2/88)	22
4801	Lippert, Lloyd LTC MS. Fibrinogen Concentration in Two Methods of Cryoprecipitate Preparation (9/88)	23
4804	Lippert, Lloyd LTC MS. Antigen Typing Reticulocytes in Mixed Red Blood Cell Populations by Flow Cytometry (10/89)	24

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DEPARTMENT OF CLINICAL INVESTIGATION (continued)		
9263	Derderian, Sarkis LTC MC. Neurohumoral Regulation of Ventilation in Patients with Elevated Adrenocorticotrophic Hormone (ACTH) and Beta Endorphins (BE) (10/85)	25
9268	Derderian, Sarkis LTC MC. Pulmonary Function in Patients with Arthritis Associated with Inflammatory Bowel Disease (5/87)	26
9271	Derderian, Sarkis LTC MC. The Ventilatory Response to Carbon Dioxide in Compensated Hepatic Cirrhosis (9/87)	27
9272	Lippert, Lloyd LTC MS. Relationship of Major Histocompatibility Complex Class II Genes to Inhibitor Antibody Formation in Hemophilia A (9/88)	28
9275	Schaudies, Paul CPT MS. Quantitation and Characterization of EGF Levels in Rat Milk (10/88)	29
9276	Schaudies, Paul CPT MS. Internalization, Proteolytic Processing and Intracellular Trafficking of 125-I-Radiolabeled Epidermal Growth Factor (EGF) in Responsive and Nonresponsive Cell Lines (10/88)	30
9278	Abdelrahim, Maged DAC. Analysis of Amino Acids in Physiological Samples by High Pressure Liquid Chromatography Using Ultrafiltration Technique (4/89)	31
9279	Sweeney, Jane COL SP. Clinical Competencies in Pediatric Physical Therapy: A Nationwide Survey of Practice (9/89)	32
9280	Derderian, Sarkis LTC MC. Sleep and Respiratory Control in Kyphoscoliosis (2/90)	33
9281	Lippert, Lloyd PhD. Relationship of Aryl Hydrocarbon Hydroxylase Activity to V-Beta T Cell Receptor Phenotype in Inbred Mouse Strains: A Model for Cancer Risk (5/90)	34

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DEWITT ARMY COMMUNITY HOSPITAL, FORT BELVOIR, VA		
8300	Cowsar, John MAJ MC. Comparison of Psyllium Plantago and Xanthan Gum in the Dietary Management of Diabetes Mellitus (1/89)	35
8301	Carr, Robert MAJ MC. Immunogenicity of a Conjugated Hemophilus Influenzae Type B Vaccine in a High Risk Geriatric Population (10/89)	36
HIV RESEARCH		
1151	Link, Christine CPT MC. Evaluation of Renal Function, Protein Excretion and the Urinary Sediment in Patients with Antibody to the Human Immunodeficiency Virus (HIV) (3/87)	37
1952	Oster, Charles COL MC. The Clinical Presentation of HIV Infected Patients at Walter Reed Army Medical Center (1/87)	38
1953	Drabick, Joseph CPT MC. The Generation of Human Monoclonal Antibodies to the HIV (1/87)	39
1958	Hoover, David LTC MC. In Situ Hybridization for Detection of HIV in Langerhans Cells of HIV Infected Patients (7/87)	40
3342	Birx, Deborah MAJ MC. Delayed Type Hypersensitivity Skin Testing: Correlation of Intradermal Injection Vs. Epicutaneous Antigen Placement and CD4 Number in Normals and HIV Seropositive Subjects (8/88)	41
4806	Anderson, David MAJ MC. Pathological Manifestations of HIV Infections at Autopsy (12/89)	42
6218	Fischer, Gerald COL MC. Evaluation of Human Immunodeficiency Virus Related Proteins on the Surface of Lymphocytes from Children with Evidence of HIV Exposure or HIV Illnesses (5/88)	43
6220	Fischer, Gerald COL MC. Epidemiology of HIV In Pediatric and Perinatal Patients - A Natural History Study (7/88)	44
6222	Fischer, Gerald COL MC. Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses (9/88)	45

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HIV RESEARCH (continued)		
6264	Pettett, Gary COL MC. Perinatal HIV Infection: Epidemiology and Natural History (4/90)	46
7128	Salazar, Andres COL MC. Neurobehavioral Consequences of HTLV-III Brain Infection and AIDS Encephalopathy (12/86)	47
7139	Salazar, Andres COL MC. Intramuscular Poly-ICLC and Zidovudine in the Management of HIV Infection: An Open Pilot Trial (7/88)	48
7243	Rundell, James MAJ MC. Psychiatric Natural History Study: Factors Related to Human Immunodeficiency Virus Transmission and Morbidity (4/90)	49
8801	Rhoads, Joanne MAJ MC. Identification and Characterization of Human Immunodeficiency Virus in Human Semen (3/88)	50
8802	Oster, Charles COL MC. VA Cooperative Study No. 298, Treatment of AIDS and AIDS Related Complex; Part I: Treatment of Patients with ARC (AZT Vs. Placebo) (4/88)	51
8803	Roberts, Chester, LTC MS. Core Protocol for HIV Developmental Diagnostics (Adults) (5/88)	52
8804	Oster, Charles COL MC. The Natural History of HIV Infection and Disease in United States Military Beneficiaries (5/88)	53
8805	Tramont, Edmund COL MC. Natural History of Oral Manifestations of HIV Infection in a United States Military Population (10/88)	54
8806	Redfield, Robert LTC MC. Active Immunization of HIV Infected Patients with Recombinant GP160 HIV Protein: Phase I Study of Immunotherapy, Immunogenicity and Toxicity (11/88)	55
8807	Drabick, Joseph CPT MC. The Use of Cimetidine for Immunoaugmentation in HIV Seropositive Patients (12/88)	56
8808	Bjornson, Darrell LTC MS. A Pharmacokinetic Study to Develop a Database to Describe the Relationship Between Zidovudine (AZT)/Glucuronyl (GAZT) Blood Levels and Drug Toxicity in HIV Infected Patients (1/89)	57

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HIV RESEARCH (continued)		
8809	Hawkes, Clifton MAJ MC. Phase I and II Study of the Use of Soluble CD4 Protein (sCD4: St4 SK&F 106528) in Human Immunodeficiency Virus Infection (1/89)	58
8810	Rhoads, Joanne MAJ MC. Factors Affecting Heterosexual Transmission of Human Immunodeficiency Virus (5/89)	59
8811	Smith, Kathleen LTC MC. The Investigation of the Cutaneous Microflora Found in HIV Infected Patients as it Relates to the Onset, Severity and Progression of Disease (5/89)	60
8812	Smith, Kathleen LTC MC. The Investigation of the Cutaneous Manifestations of HIV Infection in Relation to the Onset, Severity and Progression of Disease, Dermatologic Natural History (5/89)	61
8814	Bjornson, Darrel LTC MS. Pharmacoepidemiologic Study to Develop a Database to Document Variations in the Outcome of Illness Which May be Due to Drug Effects and To Document Patterns of Drug use in HIV Infected Patients (8/89)	62
8815	Bjornson, Darrel LTC MS. Pneumocystis Carinii Pneumonia in HIV Patients: A Cohort Study to Estimate the Protective Effect of Prophylactic Pentamidine Inhalation in Compliant Vs. Noncompliant Patients (8/89)	63
8817	Johnson, Steven MAJ MC. The Effect of HIV Infection on the Initial Manifestations and Response to Treatment of Syphilis (11/89)	64
8818	Mayers, Douglas CDR MC. Prospective Study of the Emergence of Zidovudine Resistance in Patients Infected with the Human Immunodeficiency Virus who are Treated with Zidovudine (6/90)	65
8819	Redfield, Robert LTC MC. Active Immunization of Early HIV Infected Patients with Recombinant GP160 HIV Protein: Phase II Study of Toxicity, Immunotherapy, In Vivo Immunoregulation and Clinical Efficacy (9/90)	66
8820	Redfield, Robert LTC MC. A Phase I Study of the Safety and Immunogenicity of rgp120/HIV-1-111B Vaccine in HIV-1 Seropositive Adult Volunteers (9/90)	67

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Rundell J, Brown G: HIV transmission risk behaviors and HIV-infected women: A pilot study. 37th Annual Meeting of the Academy of Psychosomatic Medicine, Phoenix, AZ, November, 1990. [7243]	Pr
Rundell J, Brown G: Persistence of psychiatric symptoms in HIV seropositive persons. Am J Psychiatry 1990;147(5):674-5. [7243]	P
Rundell J, Stasko R: Psychiatric issues in early HIV disease. 144th Annual Meeting of the American Psychiatric Association, New Orleans, LA, May, 1991. [7243]	Pr
Rundell J, Temoshok L, Tramont E: A new program for HIV behavioral medicine research within a multidisciplinary medical consortium. 12th Annual Meeting of the Society of Behavioral Medicine, Washington, DC, March, 1991. [7243]	Pr
Rundell J: Pathogenesis of HIV disease II: Neuropathology. Annual Military Medical Conference, Uniformed Services University of the Health Sciences, Bethesda, MD, October, 1990. [7243]	Pr
Rundell J: Behavioral medicine HIV research program: Five year plan. Military Medical Consortium for Applied Retroviral Research Monthly Scientific Seminar, Washington, DC, October, 1990. [7243]	Pr
Smith M, Kozjak J, Hendrix R, Temoshok L: The role of the participant in HIB biopsychosocial research. 1st International Conference on Biopsychosocial Aspects of HIV Infection, Amsterdam, The Netherlands, September, 1991. [7243]	Ab

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** P - publication, Ab - abstract, Pr - presentation

PUBLICATIONS/PRESENTATIONS BY DEPARTMENT/SERVICE AND AUTHOR

<u>CITATION*</u>	<u>TYPE**</u>
HIV RESEARCH (continued)	
Smith M: The role various patient participation mechanisms play in the medical policy and research environment. Canadian AIDS Conference, Vancouver, British Columbia, April, 1991. [7243]	Pr
Stern Y, Adams K, Butters N, Becker J, Boccellari A, Brouwers P, Campbell A, Chellune G, Heaton R, Martin A, Pequegnat W, Schmitt F, Wilkie F: Assessment of AIDS-related cognitive changes: Recommendations of the NIMH Work Group on neuropsychological assessment approaches. J Clin Exper Neuropsychol 1991;13:97. [7128]	Ab
Swango P, Kleinman D, Konzelman J: Periodontal health and immune status in HIV-infected military personnel. J Dent Res 1991;70:538. [8805]	Ab
Swango P, Kleinman D, Konzelman J: Longitudinal study of oral mucosal pathologies in HIV-infected military personnel. Abstracts of Papers, VII International Conference on AIDS, Florence, Italy, June, 1991. [8805]	Pr
Swango P, Kleinman D, Konzelman J: Oral mucosal and periodontal health in relation to immune dysfunction in HIV-infected military personnel. J Am Dent Assoc 1991;122:49-54. [8805]	P
Temoshok L, Blake S, Rundell J, Zachary R, Ostrow D: Factors predicting transmission potential in HIV-Infected individuals: Preliminary results. VII International Conference on AIDS, Florence, Italy, June, 1991. [7243]	Pr
Temoshok L, Jenkins R, Brown G, Kendall S, Patterson T: Biopsychosocial relationships in early HIV disease. 144th Annual Meeting of the American Psychiatric Association, New Orleans, LA, May, 1991. [7243]	Pr
Temoshok L, Patterson T, Blake S, Sharp E, Johnson C, Brandt U, Coyle C, Jenkins P, Chandler J: Transmission risk-relevant behaviors in HIV+ military personnel. 1st International Conference on Biopsychosocial Aspects of HIV Infection, Amsterdam, The Netherlands, September, 1991. [7243]	Ab
Temoshok L, Smith M, Brown G, Jenkins R: Perceptions of zidovudine (AZT) and cooperation with treatment or clinical trials: 1st International Conference on Biopsychosocial Aspects of HIV Infection, Amsterdam, The Netherlands, September, 1991. [7243]	Ab

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<u>CITATION*</u>	<u>TYPE**</u>
HIV RESEARCH (continued)	
Zachary R, Coyle C, Kendall S, Brown G: Living with HIV: Mechanisms for coping with psychological distress. 1st International Conference on Biopsychosocial Aspects of HIV Infection, Amsterdam, The Netherlands, September, 1991. [7243]	Ab
Zambon J, Swango P, Konzelman J: Clinical and microbiological studies of periodontal disease in HIV-infected subjects. J Dent Res 1991;70:556. [8805]	Ab
DEPARTMENT OF MEDICINE Cardiology Service	
Banks A, Laird J: Balloon aortic valvuloplasty. In: White CJ, Ramee SR, eds. Interventional Cardiology: Clinical Application of New Technologies. New York: Raven Press, 1991:199-221. [1243]	P
Echt D, Liebson P, Mitchell L, Peters R, Obias-Manno D, Barker A, Arensberg D, Baker A, Friedman L, Greene H, Huther M, Richardson D: Mortality and morbidity in patients receiving encainide, flecainide or placebo. N Engl J Med 1991;324:781-8. [1254]	P
Gaither N: Echocardiographic evaluation of stroke. Presented at the Capital Area Echo Society Meeting, Washington, DC, March, 1991. [1262]	Pr
DEPARTMENT OF MEDICINE Dermatology Service	
Tangrea J, Edwards B, Harmtna M, Taylor P: Isotretinoin-basal cell carcinoma prevential trial: Design, recruitment results, and baseline characteristics of the trial participants. Controlled Clin Trials 1990;11:433-50. [1805]	P
DEPARTMENT OF MEDICINE Endocrine-Metabolic Service	
Brennan M, Duncan W, Wartofsky L, Butler V, Wray H: In vitro dissolution of calcium carbonate preparations. Calcif Tissue Int 1991;49:308-12. [1387-87]	P
Burch H, Nagy E, Lukes Y, Cai W, Wartofsky L, Burman K: Nucleotide and amino acid homology between the human thyrotropin receptor and the HIV-1 Nef protein: Identification and functional analysis. Biochem Biophys Res Commun 1991;181(1):498-505. [1316-89]	P

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Endocrine-Metabolic Service (continued)

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| Burman K: Treatment of autoimmune ophthalmopathy. The Endocrinologist 1991;1(2):102-10. [1395-87] | P |
| Carr F, Wong N: Thyroid hormone inhibition of TSHB gene expression occurs through multiple negative TRES independent of promoter position. Endocrinology 1991;71(Suppl):125. [1393-87] | Ab |
| Carr F, Wong N: Thyroid hormone inhibition of TSHB gene expression occurs through multiple negative TRES independent of promoter position. Meeting of the American Thyroid Association, Boston, MA, September, 1991. [1393-87] | Pr |
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| Carr F: Thyroid hormone inhibits TSHB subunit gene expression independent of promoter position. Keystone Symposia, Tamarron, CO, March, 1991. [1393-87] | Pr |
| Duncan W, Glass A, Wray H: Triiodothyronine increases the hepatic and renal nuclear vitamin D receptor in castrated but not in intact male rats. J Bone Min Res 1990;5(Suppl 2):S199. [1363-85] | Ab |
| Duncan W, Glass A, Wray H: Estrogen regulation of the rat nuclear 1,25-dihydroxyvitamin D3 receptor in rat liver and kidney. Endocrinology 1991;129(5):2318-24. [1363-85] | P |
| Duncan W, Nicholson D, Wray H: mRNA for the vitamin D receptor is present in the liver. J Bone Min Res 1991;6(Suppl 1):S237. [1361-85] | Ab |
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| Francis T, Burch H, Cai W, Lukes Y, Peele M, Carr F, Wartofsky L,
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| Glass A: Use of a Y-chromosome-specific DNA probe to monitor the
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1991;12:P33. [1371-86] | Ab |
| Glass A: Use of a Y-chromosome-specific DNA probe to monitor the
albumin column method of X-Y sperm separation. American Society
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| Hicks K, Tseng Y, Lahiri S, Burman K, D'Avis J, Wartofsky L:
Identification of epidermal growth factor receptor in a cultured
medullary carcinoma cell line. Clin Res 1990;38:385A. [1399-87] | Ab |
| Humphrey M, Mosca J, Baker J, Drabick J, Carr F, Burke D, Wartofsky L,
Djuh Y, Burman K: Absence of retroviral sequences in Graves'
disease. Lancet 1991;337:17-8. [1303-88] | P |
| Norby E, Neutz J, Van Nostrand D, Burman K, Warren R: Nasal
radioiodine activity: A prospective study of frequency,
intensity, and pattern. J Nucl Med 1990;31(1):52-4. [4539] | P |
| Poth M, Tseng Y, Wartofsky L: Inhibition of TSH activation of human
cultured thyroid cells by tumor necrosis factor: An explanation
for decreased thyroid function in systemic illness. Thyroid
1991;1:235-40. [1327-90] | Ab |
| Tseng Y, Burman K, Lahiri S, Abdelrahim M, Wartofsky L: Post-binding
processing of atriopeptin (ANP) by cultured human thyroid cells:
Effect of thyrotropin. Joint Meeting of the Chinese Physiological
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natriuretic peptide receptor in cultured thyroid cells. J Clin
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DEPARTMENT OF MEDICINE

Endocrine-Metabolic Service (continued)

Tseng Y, Burman K, Lahiri S, Abdelrahim M, Wartofsky L: Post-binding processing of atriopiptin (ANP) by cultured human thyroid cells: Effect of thyrotropin. Proceedings of the American Physiological Society - Chinese Physiological Society Joint Meeting 1990;OII-1:66. [1321-90] Ab

DEPARTMENT OF MEDICINE

Gastroenterology Service

Baska R, Moses F, Deuster P: Reduction in ultramarathon running-associated gastrointestinal bleeding with cimetidine. Gastroenterology 1990;98:A19. [2031] Ab

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Larsen B: Salivary antibody response to treatment for helicobacter pylori: Preliminary data of a prospective, long-term study. Meeting of the American Gastroenterology Association, New Orleans, LA, May, 1991. [1406] Pr

Larsen B: Salivary antibody response to treatment for helicobacter pylori: Preliminary data of a prospective, long-term study. Gastroenterology 1991;99:A153. [1406] Ab

Moses F, Baska R, Kealey B, Deuster P, Peura D: Effect of cimetidine on marathon-associated gastrointestinal bleeding. Gastroenterology 1990;98:A91. [2031] Ab

Murphy J, Schaaf M, Luk G, Kikendall J, Wong R: Significant correlation between colonic mucosal ODC activity and serum somatomedin C levels in acromegaly. Gastroenterology 1991;100(5):AA389. [1416] Ab

Murphy J, Schaaf M, Luk G, Kikendall J, Wong R: Significant correlation between colonic mucosal ODC activity and serum somatomedin C levels in acromegaly. Digestive Disease Week, New Orleans, LA, May, 1991. [1416] Pr

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DEPARTMENT OF MEDICINE

Gastroenterology Service (continued)

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| Phillips R, Willis S, Luk G, Kikendall J, Bowen P, Maydonovitch C, Wong R: The effect of beta-carotene on mucosal proliferation in patients with colonic carcinoma. Gastroenterology 1991;100(5):A394. [1495] | Ab |
| Phillips R: The effect of beta-carotene on mucosal proliferation in patients with colonic carcinoma. Premalignant Conditions Research Session, American Gastroenterology Association Meeting, New Orleans, May, 1991. [1495] | Pr |
| Shay S, Eggli D, Johnson L: Simultaneous esophageal pH monitoring and scintigraphy during the postprandial period in patients with severe reflux esophagitis. Dig Dis Sci 1991;36(5):558-64. [1462] | P |
| Shay S: Ambulatory gastroduodenal 24 hr pressure and ph monitoring: An automated measurement of gastric function in man. Meeting of the American Gastroenterology Association, New Orleans, LA, May, 1991. [1498] | Pr |
| Stamm C, Maydonovitch C, Peura D: Alteration of gastric emptying by histamine H2-receptor antagonists. American College of Gastroenterology 55th Annual Scientific Meeting, San Francisco, CA, October, 1990. [1409] | Pr |
| Sullivan J, Bowen P, Kikendall J, Langenberg P, Sapuntzakis M, Burgess M, Moody S: Factors affecting serum beta-carotene levels in beta-carotene-supplemented adults. FASEB Meeting, Washington, DC, April, 1991. [1450] | Pr |
| Sullivan J, Bowen P, Kikendall J, Langenberg P, Sapuntzakis M, Burgess M, Moody S: Factors affecting serum beta-carotene levels in beta-carotene-supplemented adults. FASEB Journal 1991;5:A1073. [1450] | Ab |
| Truesdale R: Serology predicts treatment eradication of helicobacter pylori. Gastroenterology 1991;99:A176. [1406] | Ab |
| Truesdale R: Serology predicts treatment eradication of helicobacter pylori. Meeting of the American Gastroenterology Association, New Orleans, LA, May, 1991. [1406] | Pr |

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DEPARTMENT OF MEDICINE

General Medicine Service

Birdwell B, Kroenke K, Herbers J, Pangaro L, Lucas C, Noel G: Patient affect overrides objective information: A randomized trial. Clin Res 1990;38:692A. [1025] Ab

DEPARTMENT OF MEDICINE

Hematology-Oncology Service

Burrell L, Perry J, Jelinek J, Redmond J: Magnetic resonance imaging (MR) to assess extent of disease and response to treatment in small cell lung cancer (SCLC). Proceedings of the American Society of Clinical Oncology 1991;10:246. [1656-88] Ab

Burrell L, Perry J, Jelinek J, Redmond J: Magnetic resonance imaging (MR) to assess extent of disease and response to treatment in small cell lung cancer (SCLC). Meeting of the American Society of Clinical Oncology, Houston, TX, May, 1991. [1656-88] Pr

Hartman K, Wright D: Identification of autoantibodies specific for the neutrophil adhesion glycoproteins CD11b/CD18 in patients with autoimmune neutropenia. Blood 1991;78(4):1096-1104. [1639-86] P

Hartman K, Wright D: Autoantibodies to CD11B/CD18 from patients with autoimmune neutropenia alter neutrophil adhesion and opsonin receptor function in vitro. Blood 1990;76(1):182a. [1639-86] Ab

Hartman K, Wright D: Autoantibodies to CD11b/CD18 from patients with autoimmune neutropenia alter neutrophil adhesion and opsonin receptor function in vitro. Meeting of the American Society of Hematology, Boston, MA, December, 1990. [1639-86] Pr

Jelinek J, Redmond J, Perry J, Burrell L, Benedikt R, Geyer C, Peller P, Wacks L, Wise B, Ghaed V: Small cell lung cancer: Staging with MR imaging. Radiology 1990;177(3):837-42. [1656-88] P

Knight R, Perry J, Hargis J, Wright D: The use of oral mucosal neutrophil counts to follow the development and resolution of neutropenia in patients given high dose, myelosuppressive chemotherapy. Blood 1990;76:187A. [1660-88] Ab

Knight R, Perry J, Hargis J, Wright D: The use of oral mucosal neutrophil counts to follow the development and resolution of neutropenia in patients given high dose, myelosuppressive chemotherapy. Annual Meeting of the American Society of Hematology, Boston, MA, December, 1990. [1660-88] Pr

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CITATION*

TYPE**

DEPARTMENT OF MEDICINE

Hematology-Oncology Service (continued)

- La Russa V, Griffin J, Kessler S, Knight R, Wright D: Effects of anti-CD33 blocked ricin immunotoxin on the capacity of CD34+ human marrow cells to establish in-vitro hematopoiesis in long-term marrow cultures. *Exper Hematol* 1990;18(6):675. [9022-83] Ab
- La Russa V, Putnak J, Knight R: Dengue virus infection of stromal cells in Dexter cultures of human marrow. *Exper Hematol* 1991;19(6):479. [9022-83] Ab
- La Russa V, Putnak J, Knight R: Dengue virus infection of stromal cells in Dexter cultures of human marrow. *International Society of Experimental Hematology*, Parma, Italy, July, 1991. [9022-83] Pr
- Poillon W, Kark J, Kim B, Hicks C: Red cell 2,3-DPG metabolism as a target for antisickling. *Blood* 1990;76:15a. [1659-88] Ab
- Poillon W, Kark J, Kim B, Hicks C: Red cell 2,3-DPG metabolism as a target for antisickling. *Meeting of the American Society of Hematology*, San Antonio, TX, December, 1990. [1659-88] Pr
- Poillon W, Kark J, Kim B, Hicks C, Giangeruso R: Red Cell 2,3-DPG metabolism as a target for sickle cell anemia therapy. *Annual Meeting of the National Sickle Disease Program*, Mobile, AL, March, 1991. [1659-88] Pr
- Wright D, La Russa V, Knight R, Salvado A, Bednarek J: Guanine ribonucleotide metabolism and regulation of myelopoiesis. *Exper Hematol* 1991;18(6):713. [9022-83] Ab

DEPARTMENT OF MEDICINE

Nephrology Service

- Yuan C, Pamnani M, Schooley J, Moore J: Effects of thiorphan and atrial natriuretic peptide on renal function during hemorrhagic hypotension. *Physiologist* 1990;33:A93. [1152] Ab
- Yuan C, Pamnani M, Schooley J: Effects of atrial natriuretic peptide and thiorphan on renal function and renin release during hemorrhagic hypotension in rats. *J Am Soc Nephrology* 1990;1:431A. [1152] Ab

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PUBLICATIONS/PRESENTATIONS BY DEPARTMENT/SERVICE AND AUTHOR

<u>CITATION*</u>	<u>TYPE**</u>
DEPARTMENT OF MEDICINE Pulmonary Disease Service	
Derderian S, Andrada T, Culpepper W, Rajagopal K: Physiologic differences between hypoxic and non-hypoxic patients with restrictive pulmonary disease (RPD). Am Rev Respir Dis 1991;143:A192. [1711]	Ab
Derderian S, Andrada T, Culpepper W, Rajagopal K: Physiologic differences between hypoxic and non-hypoxic patients with restrictive pulmonary disease (RPD). Assembly on Respiratory Neurobiology and Sleep, Annual Meeting of the American Thoracic Society, Anaheim, CA, May, 1991. [1711]	Pr
Dillard T, Beninati W, Berg B: Air travel in patients with chronic obstructive pulmonary disease. Arch Intern Med 1991;151:1793-5. [1724]	P
Dillard T: Exercise capacity in patients with chronic obstructive pulmonary disease. Chest 1991;100:297-8. [1717]	P
Kern K, Derderian S, Rajagopal K: The response to inspiratory resistive loading in patients with restrictive lung disease. Am Rev Respir Dis 1991;143:A57. [1711]	Ab
Kern K, Derderian S, Rajagopal K: The response to inspiratory resistive loading in patients with restrictive lung disease. Annual Meeting of the American Lung Association and the American Thoracic Society, Anaheim, CA, May, 1991. [1711]	Pr
Landry F, Parker J, Phillips Y: Outcome of cardiopulmonary resuscitation in the intensive care setting. Clin Res 1991;39:580A. [1735]	Ab
Landry F, Phillips Y, Parker J: Outcome of cardiopulmonary resuscitation in the intensive care unit. Tenth Mid-Atlantic Regional Meeting of the Society of General Internal Medicine, New York, NY, March, 1991. [1735]	Pr
Landry F, Phillips Y, Parker J: Outcome of cardiopulmonary resuscitation in the intensive care unit. National Meeting of the Society of General Internal Medicine, Seattle, WA, May, 1991. [1735]	Pr

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<u>CITATION*</u>	<u>TYPE**</u>
DEPARTMENT OF MEDICINE	
Pulmonary Disease Service (continued)	
Mehm W, Dillard T, Berg B, Dooley J, Rajagopal K: Accuracy of oxyhemoglobin saturation monitors during simulated altitude exposure of men with chronic obstructive pulmonary disease. Aviation Space Environ Med 1991;62:418-21. [1724]	P
Phillips Y: Water loss without heat flux in exercise-induced asthma. Chest 1990;98(Suppl 2):128S. [1728]	Ab
Phillips Y: Water loss without heat flux in exercise-induced asthma. 56th Annual Scientific Assembly of the American College of Chest Physicians, Toronto, Canada, October, 1990. [1728]	Pr
Rajagopal K, Derderian S, Culpepper W, Andrada T: Sleep and nocturnal oxygenation in patients with restrictive pulmonary disease. Sleep Res 1991;445:20A. [1707]	Ab
Rajagopal K, Derderian S, Culpepper W, Andrada T: Sleep and nocturnal oxygenation in patients with restrictive pulmonary disease. World Congress for the Federation of Sleep Research Societies, Cannes, France, September, 1991. [1707]	Pr
NEUROLOGY SERVICE	
Kaufman H, Schwab K, Salazar A: A national survey of neurosurgical care for penetrating head injury. Surg Neurol 1991;36:370-7. [9200]	P
Salazar A: Traumatic brain injury: Pathophysiologic considerations. AIREN/PAHO Workshop on Head Injury, Costa Rica, 1991. [9200]	P
Salazar A: Invited Participant, ICRAN Workshop on Posttraumatic Epilepsy. Porto, Portugal, October, 1990. [9200]	Pr
Salazar A: Invited Participant, ICRC Working Group on the Effects of Laser Weapons. Geneva, Switzerland, November, 1990. [9200]	Pr
Salazar A: Guest Speaker and Invited Participant, 52nd National Medical Congress, Head Injury. San Jose, Costa Rica, November, 1990. [9200]	Pr
Salazar A: Invited Lecturer, Recent Advances in the Pharmacology of Head Injury and Long-Term Recovery from Head Injury: The VHIS. University of Iowa College of Nursing and the Iowa Head Injury Association, Iowa City, IA, October, 1991. [9200]	Pr

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NEUROLOGY SERVICE (continued)	
Salazar A: Invited Lecturer, HIV Dementia and Related Issues. National Kidney Foundation, Washington, DC, September, 1991. [9200]	Pr
Salazar A: Invited Participant, Consensus Conference on Guidelines for Drug Trials in Memory Disorders. Cannes, France, December, 1991. [9200]	Pr
Schwab K, Salazar A, Kaufman H: The use of an optional signature line in a survey of neurosurgeons' attitudes. Proceedings of the Meeting of the American Sociological Association, 1991. [9200]	Ab
DEPARTMENT OF PATHOLOGY AND AREA LABORATORIES	
Perry E, Moore R, Billups L, Berger T, Salata K, Lippert L: Reticulocyte persistence in stored donor blood determined by flow cytometry. Transfusion 1991;31(S96):28S. [4807]	Ab
Perry E: Reticulocyte stability in anticoagulated blood determined by flow cytometry: A report of research in progress. Mid-Atlantic Association of Blood Banks 14th Annual Meeting, Richmond, VA, April, 1991. [4807]	Pr
Perry E: Reticulocyte stability in anticoagulated blood determined by flow cytometry: A report of research in progress. Proceedings of the Mid-Atlantic Association of Blood Banks 1991:23. [4807]	Ab
DEPARTMENT OF PEDIATRICS	
Beachy J, Weisman L: The effect of asphyxia on group B streptococcal (GBS) infection in the suckling rat. Pediatr Res 1990;4:280A. [6245]	Ab
Beachy J, Weisman L: The effect of asphyxia on group B streptococcal (GBS) infection in the suckling rat. Society for Pediatric Research at the Section of Neonatal Infectious Diseases, New Orleans, LA, April, 1991. [6245]	Pr
Dykstra K, Payne M, Abdelrahim M, Francis G: In vitro effect of insulin like growth factor 1 on human neonatal foreskin fibroblasts. 73rd Annual Meeting of the Endocrine Society, Washington, DC, June, 1991. [6064]	Pr

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| Francis G, Betz J: Tumor necrosis factor (TNF) does not affect in vitro testosterone (T) production by isolated rat Leydig cells. Uniformed Services Section of the American Academy of Pediatrics, 1991. [6257] | Ab |
| Francis G, Newman R, Betz J, Poth M: Macrophage conditioned media but not tumor necrosis factor inhibits in vitro testosterone production by rat Leydig cell enriched cultures. Endocrine Society Meeting, Washington, DC, June, 1991. [6257] | Pr |
| Hachey W: Limitations in the usefulness of hematologic parameters and the urine latex particle agglutination test for group B streptococcus in the management of suspected neonatal sepsis during the first week of life. 10th Annual Conference on Military Perinatal Research, Aspen, CO, July, 1991. [6246] | Pr |
| Wiswell T, Curtis J, Dobek A, Zierdt C: Staphylococcus aureus colonization after neonatal circumcision in relation to device used. J Pediatr 1991;119(2):302-4. [6241] | P |
| Wiswell T, Curtis J, Dobek A, Zierdt C: Staphylococcus aureus colonization after neonatal circumcision in relation to device used. Pediatric Grand Rounds, Uniformed Services University for the Health Sciences, Bethesda, MD, March, 1991. [6241] | Pr |
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| Wiswell T, Hachey W: Multiple site blood cultures in the initial evaluation for neonatal sepsis during the first week of life. Pediatr Infect Dis J 1991;10:365-9. [6246] | P |
| Wiswell T, Hachey W: Early management of the meconium aspiration syndrome with either high frequency or conventional mechanical ventilation. 8th Conference on High Frequency Ventilation, Snowbird, UT, April, 1991. [6273] | Pr |
| Wiswell T, Hachey W: Early management of the meconium aspiration syndrome with either high frequency or conventional mechanical ventilation. Annual Meeting of the American Academy of Pediatrics, New Orleans, LA, October, 1991. [6273] | Pr |

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DEPARTMENT OF PEDIATRICS (continued)

Wiswell T, Hachey W: Early management of the meconium aspiration syndrome with either high frequency or conventional mechanical ventilation. *Pediatr Res* 1991;29:335A. [6273] Ab

DEPARTMENT OF PEDIATRICS
Pediatric Oncology Group

Arrigo S, Beckwith J, Sharples K, D'Angio G, Haase G: Better survival after combined modality care for adults with Wilms' tumor: A report from the National Wilms' Tumor Study. *Cancer* 1990;66(5):827-30. [6144] P

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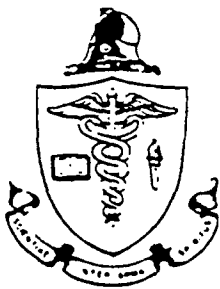
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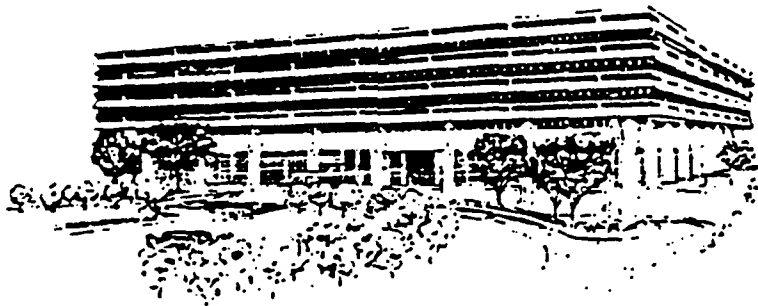
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VOLUME II

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**DEPARTMENT OF CLINICAL INVESTIGATION
WALTER REED ARMY MEDICAL CENTER
WASHINGTON, DC 20307-5001**

**CLINICAL INVESTIGATION PROGRAM
RCS MED-300(RI)**

REPORT DATE: 08/22/91

WORK UNIT # 3221

DETAIL SUMMARY SHEET

TITLE: The Role of IgG Subclasses in Hymenoptera Hypersensitivity and Immunotherapy

KEYWORDS: IgG subclasses, hymenoptera, immunotherapy

PRINCIPAL INVESTIGATOR: Engler, Renata MAJ MC

ASSOCIATES: Squire, Edward LTC MC; Salata, Kalman PhD

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 21,527 Total: \$ 21,527

STUDY OBJECTIVE

Development of a hymenoptera venom specific ELISA assay for the measurement of IgG. IgG1/2/3/4 subclasses to honey bee, wasp, yellow jacket, yellow hornet, white faced hornet. Comparison of ELISA assay with the radioimmunoassay. Comparison of venom-specific IgG and IgG-subclass levels in patients on immunotherapy versus untreated patients with a history of anaphylaxis. To follow patients on immunotherapy with serial venom specific G measurements.

TECHNICAL APPROACH

Patients are enrolled in the study during the clinic's routine bee allergy evaluation days. The parameters evaluated in each patient include: a) skin test titration with specific venoms; b) RIA testing for venom specific IgG (VS-G) and IgE; and c) ELISA assays for venom-specific G, G4 and G1. VS-G and G4 levels are followed sequentially in patients on venom immunotherapy (VIT) and compared to untreated patients. In addition, VSG and G4 levels are correlated to protection from natural sting reactions and level of severity of previous sting reactions.

PRIOR AND CURRENT PROGRESS

Two hundred and eighty patients have been enrolled to date. A sensitive and specific ELISA assay for the measurement of VS-G1, G4 and total G has been developed; both VS-G and G4 correlate well with a reputable commercial radioimmunoassay. A computerized data base has been utilized to track patients in follow-up and correlate clinical responses to venom and VS-G/G4. Patients on VIT for more than 5 years are being offered the option to stop therapy while we continue to follow their VS-G/G4 levels and monitor their natural sting rates and responses. Those patients who want to continue VIT, but at increased intervals, are maintaining protective VS-G levels.

CONCLUSIONS

VS-G levels correlate to protection against anaphylaxis in the first 3 to 4 years of venom immunotherapy (VIT). These levels decrease after 5 years of VIT, but G4 levels appear to remain elevated. VS-G4 may be a better parameter of protection even after VIT is stopped. Significant levels of VS-G are found in a subset of patients with a history of anaphylaxis and no prior VIT. Although primarily of the G4 subclass, some patients have increased VS-G1.

REPORT DATE: 04/12/91

WORK UNIT # 3336

DETAIL SUMMARY SHEET

TITLE: The Effect of Human Breast Milk Cell Supernatants on In Vitro
Immunoglobulin Secretion

KEYWORDS: breast milk, immunoglobulin

PRINCIPAL INVESTIGATOR: Moyer, Joseph MAJ MC

ASSOCIATES: Engler, Renata LTC MC; Reid, Robert COL MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Nov 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the ability of human breast milk cells in culture to continue to secrete human immunoglobulin (Ig) of all isotypes. To evaluate human breast milk cells (HBMC) supernatants (derived from cultured HBMC) in their ability to stimulate Ig secretion by peripheral blood lymphocytes (PBL).

TECHNICAL APPROACH

Human breast milk (HBM) is collected with a breast pump at 48 hours and 2-3 weeks after delivery. HBMC are separated and placed in culture for 7 days. Supernatants are harvested and assayed by isotype specific ELISA for quantitative Ig. HBMC supernatants are co-cultured with peripheral blood lymphocytes from normal donors for 8 days, and supernatants are again assayed for Ig production.

PRIOR AND CURRENT PROGRESS

Ten subjects have been enrolled in this study. The study has attempted to define optimum conditions for the assays, as well as adequate internal controls. Departure of the Principal Investigator, as well as technical difficulties (incubator with non-functional internal fans, resulting in experiments that were complicated by poor responses in the positive controls), hampered progress on this project. Illness of P.I. and Operation Desert Storm have put this project on hold at the present time.

CONCLUSIONS

Cells derived from HBM (colostrum) continue to release IgA over 7 days of culture even in the absence of any non-specific stimulation. Although IgA levels increase significantly in the first 24 hours, the HBM cells continue to secrete variable amounts of IgA over 7 days, even in serum free media. The role of lymphokines remains to be elucidated in this system.

DETAIL SUMMARY SHEET

TITLE: Comparison of House Dust Mite Educational Programs on Selected Outcome Variables

KEYWORDS: house dust mites, D.farinae, D.pteronyssinus

PRINCIPAL INVESTIGATOR: Squire, Edward LTC MC

ASSOCIATES: Huss, Karen DNSc; Salata, Kalman PhD

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 3,794 Previous FYs: \$ 0 Total: \$ 3,794

STUDY OBJECTIVE

To determine if a computerized education program about avoidance measures for house dust mite antigen leads to reduced exposure in patients with asthma.

TECHNICAL APPROACH

This is a randomized trial. Fifty-two patients were followed with symptom diaries and home visits to determine to what extent environmental measures were taken in response to practitioner's recommendation. Dust samples were collected from each home and assayed for relevant dust mite allergens, both before and after patient instructions.

PRIOR AND CURRENT PROGRESS

In 66 instances, asthmatics in the study adhered to allergist-recommendations; 17 encased mattress and box springs; 6 removed carpets; 11 removed upholstered furniture; 10 used hot water for laundering bed covers; and 22 instituted indoor temperature and humidity controls. In 44 instances, asthmatics given the experimental-computer instruction accomplished these recommendations; whereas in only 22 instances did asthmatics given conventional instruction do so ($p = .02$). Similarly, household levels of major dust mite allergens declined significantly after computer-assisted instruction; i.e., from 6.5 (SD = 7.6) ug/gm of dust to 2.2 (SD = 4.3) 12 weeks later ($p = .004$). With the exception of levels on mattresses, allergen burden did not decline after conventional instruction; i.e., 3.6 (SD = 4) before and 3.4 (SD = 5.8) after.

CONCLUSIONS

With supplementary computer-assisted instruction, more asthmatics implemented recommendations of their allergists. More successfully reduced household levels of dust mite allergens, and more experienced symptomatic improvement. However, even with these supplementary instructions, some asthmatics did nothing or improperly carried out prescribed measures. Adequate follow-up is therefore necessary.

REPORT DATE: 08/23/91

WORK UNIT # 3340

DETAIL SUMMARY SHEET

TITLE: Analysis of Carbohydrate Epitopes on Food Allergen Proteins: A Pilot Study

KEYWORDS: carbohydrate, epitopes, allergens

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Birx, Deborah MAJ MC; Engler, Renata LTC MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 7,478 Total: \$ 7,478

STUDY OBJECTIVE

A pilot study to identify and characterize carbohydrate epitopes on food allergens which react with specific IgE of patients with food allergy.

TECHNICAL APPROACH

Fluorescent enzyme linked immunosorbent assays (FELISA), sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE), isoelectric focusing (IEF), and immunoblotting are used to examine the role of carbohydrate epitopes in food allergy. Glycosidases, lectins, and purified saccharides are used to identify carbohydrate epitopes recognized by specific IgE from patients with food allergy.

PRIOR AND CURRENT PROGRESS

The relationship of IgE to food could be demonstrated in only one of the food allergic subjects, and this subject was extremely sensitive to foods. An attempt is being made to improve the sensitivity of the IgE test using allergen coupled to beads and a monoclonal anti-IgE antibody. Nine subjects have been enrolled; two controls and seven patients. There were no adverse reactions and no one withdrew from the study.

CONCLUSIONS

The assays currently employed only detect IgE at high levels, and sensitivity needs to be improved.

REPORT DATE: 08/08/91

WORK UNIT # 3341

DETAIL SUMMARY SHEET

TITLE: Occurrence of Laryngeal Dysfunction Among Patients Initially Diagnosed as Having Bronchial Asthma

KEYWORDS: asthma, laryngeal dysfunction, laryngeal dyskinesia

PRINCIPAL INVESTIGATOR: Squire, Edward LTC MC

ASSOCIATES: Moyer, Joseph MAJ MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) Define a standard approach to the evaluation of patients with suspected laryngeal dysfunction. b) Define the frequency of laryngeal dysfunction occurring with and without bronchial asthma among active duty military.

TECHNICAL APPROACH

a) Evaluate patients specifically identified as probably having laryngeal dysfunction. b) Comprehensively evaluate active duty soldiers at Walter Reed who have a profile or seek medical attention for exercise-related lung symptoms.

PRIOR AND CURRENT PROGRESS

While the diagnosis of laryngeal dyskinesia continues to be made at WRAMC, particularly among active duty soldiers evacuated from the Persian Gulf Theater for "asthma," the protocol as originally conceived has not achieved its goal of defining proportional prevalence of laryngeal dyskinesia among active duty soldiers originally diagnosed with asthma. The diagnosis of asthma is at times in error, and on other occasions the diagnosis of asthma and laryngeal dyskinesia are both warranted. Priority has also shifted towards defining what constitutes optimal management for this condition, once it is diagnosed. Thus, the next step related to this protocol will be to define a standardized, multi-option treatment approach with criteria for success or failure. The plan is to submit an addendum to this protocol, which would include a new consent form.

CONCLUSIONS

None.

REPORT DATE: 04/15/91

WORK UNIT # 3343

DETAIL SUMMARY SHEET

TITLE: Standardized Vs. Nonstandardized Allergen Products Containing Dust Mite Antigens

KEYWORDS: dust mite, potency, allergens

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Berger, Teresa BSc(MT); Hershey, Joyce BA

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 20 Previous FYs: \$ 7,354 Total: \$ 7,374

STUDY OBJECTIVE

To compare standardized and nonstandardized house dust mite allergen extracts for potency and allergen content.

TECHNICAL APPROACH

Fluorescent enzyme linked immunosorbent assay (FELISA) inhibition tests, sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE), isoelectric focusing (IEF), immunoblotting, and titrated skin prick testing are used to compare commercial allergen extracts prepared from *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* for potency and allergen content.

PRIOR AND CURRENT PROGRESS

Methods have been developed to analyze house dust mite allergens using SDS-PAGE, IEF, immunoblotting, FELISA, FELISA inhibition, and titrated house skin prick testing. A total of 13 subjects have been enrolled; four mite allergic subjects and nine normal subjects. There were no adverse reactions, no patients withdrew, and there has been no benefit to the patients. None of the serum samples collected so far contain measurable IgE against mite proteins. To improve sensitivity, new monoclonal antibody reagents are being prepared.

CONCLUSIONS

A number of in vitro and in vivo methods are being used to measure specific IgE to mite allergens. Initial results indicate that substantial differences exist between extracts from different companies. There are differences in protein content, potency, and spectrum of extract proteins. Few patients have measurable serum anti-mite IgE.

REPORT DATE: 04/18/91

WORK UNIT # 3344

DETAIL SUMMARY SHEET

TITLE: The Effect of UVB (Ultraviolet-B) Light on Immediate, Late and Delayed Hypersensitivity

KEYWORDS: ultraviolet light, skin test, allergy

PRINCIPAL INVESTIGATOR: Carpenter, Gary COL MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 5 Total: \$ 5

STUDY OBJECTIVE

To assess the effects of ultraviolet light on immediate, late, and delayed allergen skin tests. Ultraviolet-B (UVB) has been investigated as therapy of atopic dermatitis and solar urticaria and cutaneous mastocytosis. This study may help elucidate the mechanisms in which UVB is helpful in these conditions.

TECHNICAL APPROACH

Minimal erythema dose will first be determined. The patient will then receive 1 and 2 MED and MED applied to different randomized areas of the back. The patient is then skin tested at 15 minutes, 24 hours, or 72 hours, and the skin tests are read.

PRIOR AND CURRENT PROGRESS

Eleven patients have been studied in group 1 (skin testing right after UV radiation), and one patient has been studied 24 hours after UV radiation (group 2). Due to the loss of Dr. Samlaska to graduation and the war in the Middle East, progress has slowed. Dr. Saad has volunteered to take over for Dr. Samlaska. At least five more patients will be sought for group 1. The study may then be terminated because of the discomfort of skin testing experienced by one patient 24 hours after UV radiation. The data on the first six patients in group 1 was presented at the American Academy of Allergy and Immunology in March 1990 and was published as an abstract in the January 1990 issue of Journal of Allergy and Clinical Immunology. No subject has withdrawn from the study. This study does not benefit the patient.

CONCLUSIONS

At least five more patients need to be studied in group 1 before this study can be terminated. With 16 patients, there should be adequate statistical power to demonstrate clinically and statistically significant effects of UV light on cutaneous reactions to antigen. Groups 2 and 3, who are skin tested 24 or 48 hours after UV radiation, will require somewhat lower doses of UV light to reduce their discomfort. This will require a minor change in protocol.

REPORT DATE: 04/05/91

WORK UNIT # 3345

DETAIL SUMMARY SHEET

TITLE: Cross Allergenicity of Pollen Allergens from American Linden and European Linden

KEYWORDS: linden, pollen, cross reactivity

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA; Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 330 Total: \$ 330

STUDY OBJECTIVE

To compare the cross allogenicity of pollen from American linden and European linden trees.

TECHNICAL APPROACH

Fluorescent enzyme linked immunosorbent inhibition assays (FELISA), sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE), isoelectric focusing (IEF), and immunoblotting are used to compare cross allergenicity between American linden and European linden pollen.

PRIOR AND CURRENT PROGRESS

Methods have been developed to measure linden pollen protein in immunoassay techniques and in polyacrylamide gels. One and two dimensional techniques using extracts and pollen have also been developed. Little or no IgE directed against linden protein has been uncovered. Four patients enrolled; no subjects withdrew; there were no adverse reactions.

CONCLUSIONS

Several methods have been developed to analyze linden proteins. Little physiochemical difference was found between the pollen proteins from the two species. Substantial differences exist between proteins in commercial extracts and in whole pollen. Little anti-linden IgE was found in linden allergic's serum. Perhaps a monoclonal anti-human IgE will improve sensitivity of the immunoassay; this is being explored. IgE may be also mostly sequestered on mast cells.

REPORT DATE: 07/05/91

WORK UNIT # 3346

DETAIL SUMMARY SHEET

TITLE: Comparison of Three Methods of Assessing Induction of Mitogen and Allergen Specific Lymphocyte Proliferation

KEYWORDS: lymphocyte, proliferation, fluorescence

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 79 Previous FYs: \$ 1,462 Total: \$ 1,541

STUDY OBJECTIVE

To compare three methods of measuring lymphocyte proliferation induced by dust mite allergens and lymphocyte mitogens.

TECHNICAL APPROACH

Cell counting with a Coulter counter, fluorescein release and 3H-thymidine incorporation are used to measure lymphocyte proliferation in response to allergens and mitogens. The methods are compared for sensitivity; 3H-thymidine acts as the gold standard.

PRIOR AND CURRENT PROGRESS

A method has been developed to quantitate cells in culture which is based on fluorescein release from fluorescein diacetate. An especially appealing aspect of this assay is that cells directly from culture may be used; it is not necessary to wash the cells which greatly simplifies the assay. The color of plate used in the assay is important; a 32-fold increase in sensitivity can be achieved by using white plates in the assay. Neither the counting nor fluorescein release method is as good as the 3H-thymidine incorporation method. One normal subject has been enrolled. There were no adverse reactions, no patients withdrew, and there was no benefit to the patients.

CONCLUSIONS

In preliminary studies the 3H-thymidine incorporation method appears to be the best method for measuring lymphocyte proliferation. If further experiments support this conclusion, the protocol will be terminated. A simple fluorescent assay for quantitating cultured cells was developed. A way of greatly increasing the sensitivity of 96 well plate fluorescent assays was demonstrated.

REPORT DATE: 08/23/91

WORK UNIT # 3347

DETAIL SUMMARY SHEET

TITLE: A Simple Prick Puncture End Point Titration Procedure to Evaluate the Safety of Switching from Nonstandardized to Standardized Allergen Extracts for Use in Immunotherapy

KEYWORDS: skin test, allergens, immunotherapy

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Squire, Edward LTC MC; Cambre, Daniel MAJ MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 40 Total: \$ 40

STUDY OBJECTIVE

To evaluate safety and validity of a simplified skin prick puncture end-point procedure for switching between non-standardized and standardized mite extracts.

TECHNICAL APPROACH

Titrated end-point skin prick puncture tests with mite extracts are employed.

PRIOR AND CURRENT PROGRESS

Six subjects have been enrolled and tested, and the results have been submitted to Dr. Seltzer who is compiling results.

CONCLUSIONS

The test seems simple enough, but the final results have not been tabulated, so no final conclusions can be drawn.

REPORT DATE: 06/01/91

WORK UNIT # 3348

DETAIL SUMMARY SHEET

TITLE: Immunotherapy Reactions

KEYWORDS: allergy immunotherapy, venom immunotherapy, adverse reactions

PRINCIPAL INVESTIGATOR: Engler, Renata LTC MC

ASSOCIATES: Smith, Laurie MD; Carpenter, Gary MD

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To maintain a data base of the results of an ongoing chart audit of all patients receiving immunotherapy (IT) at Walter Reed Army Medical Center since 1986. To establish the incidence of different types of adverse reactions in relation to the following parameters: Number of injections received of increasing or maintenance IT, specific extract contents, nature of all reactions and underlying patient factors (e.g. beta blockers).

TECHNICAL APPROACH

A weekly chart review will be conducted of all patients having received IT at WRAMC Allergy Clinic. Reactions are categorized into three levels of local reactions as well as cutaneous/systemic anaphylaxis. Data is entered into a computer data base for analysis.

PRIOR AND CURRENT PROGRESS

More than 20,000 injections administered to over 150 patients have been tabulated since 1986. Because of Operations Desert Shield/Storm and a shortage of personnel for data entry, there is currently a backlog to 1990. It is anticipated that the data base will be brought up to date in 1991.

CONCLUSIONS

1) Increasing IT had significantly more systemic reactions than maintenance IT for both inhalant allergens and venom. 2) Specific aeroallergen (AA) IT reactions were not correlated to extract type/content. 3) Venom IT had a significantly lower rate of reaction for all three categories of local reactions (compared to AA IT, $p < 0.001$) but was not statistically different for systemic reasons.

REPORT DATE: 03/29/91

WORK UNIT # 3349

DETAIL SUMMARY SHEET

TITLE: Mitogen-Inducible T Suppressor Cell Assay by Flow Cytometry

KEYWORDS: activation, flow cytometry, suppressor

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA, Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 2,763 Previous FYs: \$ 0 Total: \$ 2,763

STUDY OBJECTIVE

To measure T cell suppression using a lymphocyte activation marker. To measure the suppression of mitogen stimulated lymphocytes of concanavalin A induced lymphocyte proliferation by two color flow cytometry.

TECHNICAL APPROACH

Suppression will be measured by culturing activated suppressor lymphocytes (effectors) with target lymphocytes and then measuring a parameter of activation of the targets. Lymphocyte activation will be assessed by measuring CD69 expression on the lymphocyte membrane using a monoclonal antibody. Target cells will be stained with a fluorescent vita stain, DIO, to identify them. CD69 expression will be used to assess suppression of lymphocyte activation caused by mitogen induced suppressor cells. Flow cytometry will be used to make these measurements.

PRIOR AND CURRENT PROGRESS

A two color flow cytometric method was developed to measure mitogen induced suppressor cell function. DIO is a useful reagent for use in assays which involve mixes of more than one group of cells which must be monitored individually. CD69 in lymphocyte expression begins to appear within hours of stimulation, peaks at 18 hours, and remains elevated. Suppressor cell function was measured in a number of normal subjects. Seventeen subjects were enrolled; no adverse reactions occurred.

CONCLUSIONS

This assay greatly improves and expands activated suppressor cell function compared to older methods. Harsh treatments of effectors and radioactive materials are avoided. The cells are allowed to function in a more natural way. This method will allow other parameters of the lymphocytes to be measured simultaneously.

REPORT DATE: 04/19/91

WORK UNIT # 3350

DETAIL SUMMARY SHEET

TITLE: Flow Cytometric Analysis of Natural Killer Cell Activity and Antibody-Dependent Cell-Mediated Cytotoxicity

KEYWORDS: flow cytometry, natural killer cells, cytotoxicity

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA; Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 40 Previous FYs: \$ 0 Total: \$ 40

STUDY OBJECTIVE

To measure in vitro natural killer (NK) cell activity and antibody-dependent cell cytotoxicity (ADCC) against cultured tumor cell lines using a 2-color flow cytometric assay.

TECHNICAL APPROACH

The assay uses peripheral blood mononuclear cells from normal subjects as effector cells and tumor cells as targets. Target cells are stained with a fluorescent dye, 3,3'-diiododecylcarboxycyanine perchlorate, to distinguish them from effector cells. Killed cells are identified using propidium iodide which stains dead cells. ADCC is measured using antibody coated cells, NK activity is measured using uncoated cells. Measurements are performed with a flow cytometer. Forward light scatter, side scatter, and two colors of fluorescent light are measured.

PRIOR AND CURRENT PROGRESS

An assay has been devised and tried on two subjects so far. Some variability was seen, and final conclusions will have to wait until the study is concluded. It was possible to measure dead target cells, and it also appears possible to measure residual intact target cells. In some cases it appeared that the targets were not just dead but disintegrated. A shorter incubation period may be necessary. There have been no adverse reactions, and no one has withdrawn from the study.

CONCLUSIONS

A killer cell assay has been developed and tried in preliminary experiments. Whether quantitation of dead target cells or residual intact target cells is the best way to assess cell killing remains to be seen. It is true, however, that the flow cytometer gives much more information than older methods of measuring killer cell activity.

REPORT DATE: 04/22/91

WORK UNIT # 3351

DETAIL SUMMARY SHEET

TITLE: In Vitro House Dust Mite Allergy Assays: Comparison of a Monoclonal Antibody/Allergen Capture Method with a Fluorescent Allergosorbant Test

KEYWORDS: allergy, IgE, monoclonal

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA; Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 271 Previous FYs: \$ 0 Total: \$ 271

STUDY OBJECTIVE

To compare two in vitro methods of detecting house dust mite allergy in normal and proven allergic subjects. To measure IgE directed against D. farinae F1 and D. pteronyssinus P1 proteins by monoclonal antibody/allergen capture and mite specific IgE by a FAST method.

TECHNICAL APPROACH

The FAST assay uses antigen coated plates in a fluorescent enzyme-linked immunosorbent assay. The capture assay employs monoclonal antibodies directed against allergen proteins. These monoclonal antibodies are used to capture allergens from a complex extract. Serum from volunteers is exposed to these immobilized allergens to detect the presence of anti-house dust mite IgE.

PRIOR AND CURRENT PROGRESS

Methods have been developed to analyse IgE directed against house dust mite allergens F1 and P1 using a fluorescent enzyme-linked immunosorbent assay and a monoclonal antibody capture method. None of the serum samples collected so far contained measurable IgE against mite proteins. To improve sensitivity new monoclonal antibody reagents are being prepared. A total of 19 subjects have been enrolled; 10 mite allergic subjects and 9 normal subjects. There were no adverse reactions, no patients withdrew, and there were no benefits to the patients.

CONCLUSIONS

Two in vitro methods were used to measure IgE specific to mite allergens. In initial studies none of the mite sensitive patients had measurable serum anti-mite IgE. Whether this is due to the sensitivity of the test or because the IgE is sequestered on mast cells is unclear. New monoclonal antibody reagents are being prepared to improve the sensitivity of the test.

REPORT DATE: 03/21/91

WORK UNIT # 3352

DETAIL SUMMARY SHEET

TITLE: Use of Steroid Sparing Agents Among Asthmatics Doing Poorly on
Corticosteroids: A Pilot Study

KEYWORDS: asthma, methotrexate

PRINCIPAL INVESTIGATOR: Squire, Edward LTC MC
ASSOCIATES: Lombardo, Fredric MAJ MS

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 1,439 Previous FYs: \$ 0 Total: \$ 1,439

STUDY OBJECTIVE

To establish a consensus as to rational treatment approach for severe, steroid-dependent asthma at Walter Reed Army Medical Center.

TECHNICAL APPROACH

The definition of success/failure of asthma control will be based upon seven indicators: symptoms; mini-peak flows; PRN use of bronchodilators; lung function; asthma admissions; quality of life; and willingness of physician/patient to continue treatment. We used this definition to prospectively judge the outcome of 30 open-treatment trials among 19 steroid-dependent asthmatics, all of whom were doing poorly with conventional management. The three treatment regimens were: 3 months of weekly MTX, 10-30 mg, im or po; qod maintenance TAO, 250 mg/4 mg po; and up to 6 months of daily Gold 3 mg po bid.

PRIOR AND CURRENT PROGRESS

MTX proved to be successful in controlling asthma in nine trials, in contrast with only three successful trials when using a maintenance (250 mg/4 mg) dose of TAO; higher TAO doses have not averted steroid-morbidity. Of the eight TAO failures, four succeeded with the administration of MTX, and of the two Gold failures, one succeeded with MTX. However, seven trials of MTX failed because of: nausea, patient stopped MTX; nausea, vomiting, transaminitis, physician's or patient's discontinuation of MTX; recurrent infection (2 UTI's, cellulitis), or insufficient improvement in asthma control (four patients). Of the last four failures, one succeeded after three more months of MTX. Two others remained failures despite receiving the maximum tolerated doses (oral mucositis, nausea, vomiting) for an additional 4 and 13 months.

CONCLUSIONS

Overall, we are encouraged by these results obtained with the use of MTX, and therefore continue to study this regimen. However, in view of the seven failures experienced with this treatment, we have begun to seek alternatives. Improved therapy for adrenal corticosteroid-dependent asthma continues to be sorely and urgently needed!

REPORT DATE: 05/22/91

WORK UNIT # 3353

DETAIL SUMMARY SHEET

TITLE: Contrasuppressor Cells in Allergy Immunotherapy

KEYWORDS: flow cytometry, contrasuppressor, immunotherapy

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA; Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 530 Previous FYs: \$ 0 Total: \$ 530

STUDY OBJECTIVE

To measure contrasuppressor T cells in individuals with multiple allergies who are on high and low dose immunotherapy with allergen extracts. Measurements will also be performed on cells from normal and untreated allergic subjects.

TECHNICAL APPROACH

Flow cytometry will be used to measure fluorescently labeled V. villosa lectin to lymphocytes.

PRIOR AND CURRENT PROGRESS

In preliminary studies using cells on hand the lectin bound to all lymphocytes. No subjects have been enrolled.

CONCLUSIONS

Unlike reports in the literature which indicate that a small population of lymphocytes binds V. villosa lectin, in preliminary studies it was found that all lymphocytes bound this lectin. A commercially prepared, directly labelled lectin was used in this work. Other groups have used a biotinylated lectin followed by avidin-FITC which may explain the difference. A biotinylated lectin will be prepared and compared to the directly labelled lectin.

REPORT DATE: 06/13/91

WORK UNIT # 3354

DETAIL SUMMARY SHEET

TITLE: Two Way Mixed Lymphocyte Culture: Analysis by Two Color Flow Cytometry

KEYWORDS: MLC, flow cytometry, DIO

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA; Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 3,344 Previous FYs: \$ 0 Total: \$ 3,344

STUDY OBJECTIVE

To devise a two-color, simultaneous, two-way mix lymphocyte culture assay.

TECHNICAL APPROACH

Flow cytometry will be used to measure lymphocyte activation in two-way mixed lymphocyte cultures. Cell surface expression of CD69 will be used as a measure of lymphocyte activation. A fluorescent vital stain, 3,3'-dioctadecyloxacarbocyanine perchlorate, will be used to differentiate the cell populations.

PRIOR AND CURRENT PROGRESS

The assay has been established using a purified anti-CD69 antibody and a PE-labeled second antibody. Fourteen subjects have been enrolled. No adverse reactions have occurred; no subjects have withdrawn.

CONCLUSIONS

An assay of the mixed lymphocyte reaction base on flow cytometry and a fluorescent vital stain have been developed. Unlike other methods both populations of cells may be analyzed simultaneously and the harsh treatments of current methods are avoided. The cells are allowed to function in a much more natural fashion and additional analyses are possible which are not possible using current methods.

REPORT DATE: 06/06/91

WORK UNIT # 3355

DETAIL SUMMARY SHEET

TITLE: Effect of Methotrexate on Expression of Intercellular Adhesion Molecule I in Interleukin-1 Stimulated Cultured Human Cells

KEYWORDS: methotrexate, interleukin-1, ICAM-1

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

ASSOCIATES: Hershey, Joyce BA; Berger, Teresa BSc(MT)

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 205 Previous FYs: \$ 0 Total: \$ 205

STUDY OBJECTIVE

To measure the effect of methotrexate on interleukin-1 induced ICAM-1 expression in cultured human fibroblasts and adenocarcinoma cells.

TECHNICAL APPROACH

Expression of ICAM-1 is measured using monoclonal antibodies, flow cytometry, and enzyme-linked immunosorbent assay.

PRIOR AND CURRENT PROGRESS

Cultured cells were incubated with IL-1 to stimulate ICAM-1 expression. In general the cells responded well, and the ICAM-1 was readily detectable with monoclonal antibodies and flow cytometry. Concurrent incubation of cells with methotrexate and IL-1 did not effect IL-1 induced ICAM-1 expression.

CONCLUSIONS

An IL-1 induced ICAM-1 expression assay was established. Methotrexate does not effect ICAM-1 expression in this system. The anti-inflammatory actions of methotrexate do not appear to be mediated by inhibition of IL-1 induced ICAM-1 expression.

REPORT DATE: 08/16/91

WORK UNIT # 3356

DETAIL SUMMARY SHEET

TITLE: High Dose Intravenous Immunoglobulin in the Treatment of Chronic
Inflammatory Demyelinating Polyneuropathy

KEYWORDS: intravenous, immunoglobulin, CIDP

PRINCIPAL INVESTIGATOR: Davis, William CPT MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the clinical and immunologic benefits of high dose intravenous immunoglobulin (IVIG) in the treatment of chronic inflammatory demyelinating polyneuropathy.

TECHNICAL APPROACH

Single arm design with patients receiving placebo, then active treatment with IVIG.

PRIOR AND CURRENT PROGRESS

This protocol has not been approved by HSC for acceptance of the gift of IVIG from Sandoz Pharmaceuticals. In all likelihood, this project will be cancelled.

CONCLUSIONS

None.

REPORT DATE: 09/03/91

WORK UNIT # 3357

DETAIL SUMMARY SHEET

TITLE: Serum and Secretory Immune Status of Patients with Chronic Sinusitis and Normals

KEYWORDS: sinusitis, immunodeficiency, mucosal immunity

PRINCIPAL INVESTIGATOR: Lieberman, Alan CPT MC

ASSOCIATES: Engler, Renata LTC(P) MC

SERVICE: Allergy-Immunology Service

STATUS: Ongoing

APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 3,533 Previous FYs: \$ 0 Total: \$ 3,533

STUDY OBJECTIVE

To evaluate the humoral, cellular, and mucosal immune responses of patients with chronic sinusitis in comparison with normal controls.

TECHNICAL APPROACH

Functional humoral immunity will be assessed by measuring total and antigen-specific antibody levels. Pre/post immunization with tetanus/diphtheria/H influenza type b and Pneumovac will be given. Cellular immune function will be evaluated using delayed hypersensitivity skin testing, lymphocyte phenotyping and in vitro lymphocyte functional assays; mucosal immune function will be measured by collection of nasal secretions in response to methacholine and histamine; and IgG, IgA, secretory IgA, lactoferrin, lysozyme and albumin measurements will be analyzed.

PRIOR AND CURRENT PROGRESS

Investigators have been trained in technique of nasal challenge and secretion collection. Normal controls and one patient with sinusitis have been studied. ELISA assays for measurement of components of nasal secretions are being standardized. Presently, a data base for study information is being developed.

CONCLUSIONS

There is insufficient data for definitive conclusions at this time. Procedure of nasal challenges have been well tolerated.

REPORT DATE: 09/06/91

WORK UNIT # 3358

DETAIL SUMMARY SHEET

TITLE: Plasma Level of Mast Cell Tryptase in Patients Undergoing
Immunodiagnostic or Immunotherapy Procedures who Experience Adverse
Reactions

KEYWORDS: Tryptase, Anaphylaxis, Mast Cell

PRINCIPAL INVESTIGATOR: Salata, Kalman PhD

SERVICE: Allergy-Immunology Service

STATUS: Ongoing
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 2,097 Previous FYs: \$ 0 Total: \$ 2,097

STUDY OBJECTIVE

To measure tryptase levels in blood samples from patients in the Allergy/Immunology Clinic who experience local or systemic reactions in response to diagnostic or immunotherapy procedures.

TECHNICAL APPROACH

Immunoassays are used to measure mast cell tryptase levels in blood samples from subjects who have experienced a reaction as well as from subjects who have not had a reaction. Samples are drawn at the time of the reaction and a period of days later. The second sample acts as a baseline sample. Control subjects have samples drawn in a similar manner with a similar time period between samples.

PRIOR AND CURRENT PROGRESS

The immunoassay works well. To date, all samples have been negative for tryptase. The assay works with controls and standards. Ten normal subjects and 16 subjects with a variety of reactions have been enrolled. The reactions suffered by these patients have been on the mild end of the systemic reaction scale. There have been no adverse reactions and no subject has withdrawn from the study.

CONCLUSIONS

An assay for mast cell tryptase has been established in the laboratory. To date, all samples from subjects who suffered a reaction have been negative for tryptase. There have been no false positives. It appears that only vigorous anaphylactic reactions produce measurable levels of tryptase in the blood. This test, at the moment, does not appear to be of much utility in diagnosing the milder systemic allergic reactions.

REPORT DATE: 04/24/91

WORK UNIT # 2584

DETAIL SUMMARY SHEET

TITLE: Evaluation of Patients with Obstructive Sleep Apnea Syndrome Following Uvulopalatopharyngoplasty

KEYWORDS: obstructive sleep apnea, uvulopalatopharyngoplasty, polysomnography

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

ASSOCIATES: Culpepper, William DAC; Rajagopal, Krishnan LTC MC

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing

APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 2,858 Total: \$ 2,858

STUDY OBJECTIVE

To study the perioperative risk following uvulopalatopharyngoplasty (UPPP) for obstructive sleep apnea patients, and how psychological test results are affected by surgery.

TECHNICAL APPROACH

Patients are selected for surgery based on clinical and polysomnographic parameters. Patients will be administered polysomnography on the night before surgery, night of surgery, night after surgery, and 3 months following surgery. Sleep parameters, disordered breathing, and oxygenation parameters are compared across studies looking at known perioperative risk factors (i.e., do they worsen or improve). Clinical response to UPPP and psychological status are recorded between the first and last night's assessments.

PRIOR AND CURRENT PROGRESS

To date, 20 patients have been evaluated, 18 of which have provided useable data. Six abstracts have been presented or accepted for presentation at major national and international scientific meetings. One manuscript is currently being reviewed for publication in a refereed scientific journal. The data continues to suggest that patients with nocturnal oxygen saturations > 80% are at little risk for complications in the immediate postoperative period. Patients with a pre-UPPP oxygen saturation </- 80%, while not at a statistically significant increased risk for complications, do show more complications and initial adverse response to the surgery. At three months following surgery, patients show significant improvement in mood and depression using standardized psychological measures.

CONCLUSIONS

While data are still being accumulated, several general conclusions can be drawn: 1) UPPP generally has beneficial effects on sleep and mood; 2) patients undergoing UPPP with pre-UPPP oxygen saturations </- 80% should be monitored on a standard ward for at least 48 hours; and 3) at 3 months following UPPP about 50% of patients show a clinical response (i.e., no further treatment warranted), but we have not identified a reliable factor to predict which patients will respond.

REPORT DATE: 08/12/91

WORK UNIT # 4801

DETAIL SUMMARY SHEET

TITLE: Fibrinogen Concentration in Two Methods of Cryoprecipitate Preparation

KEYWORDS: cryoprecipitate, fibrinogen, factor VIII

PRINCIPAL INVESTIGATOR: Lippert, Lloyd LTC MS

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine if a relationship exists between loss of fibrinogen and factor VIII and the volume of supernatant plasma removed during the preparation of cryoprecipitate from fresh frozen plasma; and b) If a relationship exists, what the relationship is and whether the information could be used to improve yield of fibrinogen and factor VIII in cryoprecipitate.

TECHNICAL APPROACH

Collect aliquots of supernatant plasma at predetermined intervals as the supernatant plasma was removed. Measure fibrinogen and factor VIII content of these aliquots and compare to the content in the starting plasma and final product. Two methods of cryoprecipitate preparation were studied and compared. Utilize linear regression to determine if linear relationship exists between constituent and volume of supernatant plasma.

PRIOR AND CURRENT PROGRESS

One hundred twenty-three units of cryoprecipitate were prepared, 61 by the "quick thaw" method and 62 by the "slow thaw" method. Factor VIII and fibrinogen yields were calculated and yield from the two methods compared. Furthermore, linear regression analysis was utilized to determine the relationship of the yield of the two constituents, factor VIII and fibrinogen, and the volume of the two constituents, factor VIII and fibrinogen, and the volume of the final product.

CONCLUSIONS

Yields of both factor VIII and fibrinogen were significantly greater and volume of final product was significantly lower for the "slow thaw" prepared product. The original sampling strategy did not, however, allow determination of the relationship between the final volume and yields of the two analytes in the "slow thaw" product.

REPORT DATE: 04/12/91

WORK UNIT # 4804

DETAIL SUMMARY SHEET

TITLE: Antigen Typing Reticulocytes in Mixed Red Blood Cell Populations by Flow Cytometry

KEYWORDS: flow cytometry, reticulocyte, red cell antigens

PRINCIPAL INVESTIGATOR: Lippert, Lloyd LTC MS

ASSOCIATES: Griffin, Gary CPT MS; Salata, Kalman PhD

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To develop a procedure to determine the red cell antigen phenotype of a recently transfused patient using a sample containing both patient and donor blood.

TECHNICAL APPROACH

The approach being developed is a dual staining technique followed by analysis with a flow cytometer. The presence or absence of a particular red cell antigen is detected using the fluorescent stain phycoerythrin (PE) in an indirect antiglobulin procedure. Reticulocytes are stained with a second fluorescent stain, thiazole orange (TO). If you assume that the reticulocytes are from the patient, then the phenotype of the reticulocyte is the patient's phenotype.

PRIOR AND CURRENT PROGRESS

Reticulocyte identification and antigen phenotyping were performed on 319 mixed red blood cell (MRBC) samples prepared from CPDA-1 anticoagulated donor cells and untransfused patient cells in all c(hr') antigen combinations. The flow cytometry profiles allowed clear differentiation between antigen negative and positive cells whether they were the major (75%) or the minor (25%) population. Nearly identical results were obtained in similar experiments with anti-Rho, -K, -Fya, -Fyb, and -Jka. Nineteen patients were tested with an expanded panel of nine antisera. Eighty-seven percent of the flow cytometer results agreed with results from manual testing. Of the 20 inconclusive results, five were in a patient with a very low reticulocyte count and another five were with anti-S. No false positive results were recorded.

CONCLUSIONS

A simple dual color flow cytometry procedure was developed which correctly determines the red cell antigen phenotype of the transfused patient. It was successfully applied to patients who received a single unit of antigen mismatched blood and to patients who were either chronically or massively transfused.

REPORT DATE: 06/10/91

WORK UNIT # 9263

DETAIL SUMMARY SHEET

TITLE: Neurohumoral Regulation of Ventilation in Patients with Elevated
Adrenocorticotrophic Hormone (ACTH) and Beta Endorphins (BE)

KEYWORDS: beta endorphine, CRH, respiratory control

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing

APPROVAL DATE: Oct 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,446 Total: \$ 1,446

STUDY OBJECTIVE

To examine the role of B-endorphine and other neuropeptides in the regulation of respiration.

TECHNICAL APPROACH

To noninvasively assess respiratory function during hypercapnic rebreathing in patients with Addison's disease. Assessments will be performed on four successive days -- a baseline assessment and after administration of naloxone, placebo, and dexamethasone.

PRIOR AND CURRENT PROGRESS

Because Addison's disease is an uncommon condition, we have been able to evaluate only one patient every year or two. To date, we have studied six patients. The data is insufficient to make any meaningful conclusions, with the exception that as a group these patients appear to have a reduced ventilatory response to carbon dioxide. There has been no incidence of serious or unexpected adverse reactions.

CONCLUSIONS

None to date.

REPORT DATE: 07/11/91

WORK UNIT # 9268

DETAIL SUMMARY SHEET

TITLE: Pulmonary Function in Patients with Arthritis Associated with
Inflammatory Bowel Disease

KEYWORDS: pulmonary function, arthritis, bowel disease

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Clinical Investigation

STATUS: Completed

APPROVAL DATE: May 1987

FUNDING: Current FY: \$ 683 Previous FYs: \$ 5,881 Total: \$ 6,564

STUDY OBJECTIVE

To evaluate pulmonary function in patients with inflammatory bowel disease (IBD) with arthritis and compare them to patients with IBD without arthritis.

TECHNICAL APPROACH

Using full pulmonary function tests (PFT), to include ABG's and compliance studies, we plan to compare the above two groups with regard to their respiratory function.

PRIOR AND CURRENT PROGRESS

This study is being terminated due to the difficulty of enrolling patients during acuteness of disease.

CONCLUSIONS

None.

REPORT DATE: 09/26/91

WORK UNIT # 9271

DETAIL SUMMARY SHEET

TITLE: The Ventilatory Response to Carbon Dioxide in Compensated Hepatic Cirrhosis

KEYWORDS: GABA, respiratory control, cirrhosis

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing
APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 695 Previous FYs: \$ 12,446 Total: \$ 13,141

STUDY OBJECTIVE

To examine the potential role for gamma-aminobutyric acid (GABA) in the regulation of respiration.

TECHNICAL APPROACH

To noninvasively assess respiratory function and the pattern of breathing during hypercapnic rebreathing in subjects with cirrhosis of the liver and in normal controls.

PRIOR AND CURRENT PROGRESS

We have studied 11 cirrhotic subjects to date and have demonstrated a significant reduction in hypercapnic ventilatory response in these subjects compared to controls. Because the Gastroenterology Service does not perform many liver biopsies, stable cirrhotic patients are difficult to find. Completion of the study is anticipated within the next 12 to 19 months.

CONCLUSIONS

There is evidence of a reduced hypercapnic ventilatory response in subjects with stable cirrhosis.

REPORT DATE: 09/06/91

WORK UNIT # 9272

DETAIL SUMMARY SHEET

TITLE: Relationship of Major Histocompatibility Complex Class II Genes to Inhibitor Antibody Formation in Hemophilia A

KEYWORDS: inhibitor, hemophilia A, histocompatibility

PRINCIPAL INVESTIGATOR: Lippert, Lloyd LTC MS

ASSOCIATES: Fisher, Lyman MD PhD

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing

APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 1,802 Previous FYs: \$ 33,643 Total: \$ 35,445

STUDY OBJECTIVE

To identify a marker or trait which will prospectively identify the Hemophilia A subpopulation at risk for developing anti-factor VIII inhibitor antibodies, and to substantiate a statistical association between the inhibitor phenotype and the major histocompatibility complex (MHC) using HLA testing.

TECHNICAL APPROACH

The HLA phenotypes of both inhibitor and non-inhibitor hemophilia patients will be determined by microlymphocytotoxicity. Restriction fragment length polymorphism (RFLP) analysis will be performed on peripheral blood DNA digested with a battery of restriction enzymes, Southern blotted, and probed with class II MHC alpha and beta gene probes.

PRIOR AND CURRENT PROGRESS

From August 1990 through August 1991, six patients resubmitted blood samples for HLA phenotyping and five additional hemophilia patients enrolled in the study and were HLA typed, bringing the total number of patients in the study to 45. DNA was extracted from peripheral blood lymphocytes on 18 patients during this same period.

CONCLUSIONS

An insufficient number of patients have been accessioned to initiate complete data analysis.

REPORT DATE: 03/08/91

WORK UNIT # 9275

DETAIL SUMMARY SHEET

TITLE: Quantitation and Characterization of EGF Levels in Rat Milk

KEYWORDS: EGF, milk

PRINCIPAL INVESTIGATOR: Schaudies, Paul CPT MS

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 374 Previous FYs: \$ 16,417 Total: \$ 16,791

STUDY OBJECTIVE

To examine the levels of epidermal growth factor (EGF) present in rat milk. To identify immunoreactive species of EGF and determine relationship to standard r-EGF. To characterize forms regarding their biological activities in vitro.

TECHNICAL APPROACH

Radioimmunoassay of diluted whole rat milk. Generation of an affinity resin against rat EGF. Affinity extraction of immunoreactive material in milk. Native polyacrylamide gel electrophoresis of affinity purified materials. Extraction of activity from gels. Assay of activity for receptor binding and induction of DNA synthesis.

PRIOR AND CURRENT PROGRESS

Levels of immunoreactive growth factor in lactating rats starts at approximately 5 ng/ml and rises to 30 ng/ml by day 4. This level is maintained until pups are weaned at around day 25. Native polyacrylamide gel electrophoresis of affinity isolated immunoreactive material indicated the presence of three distinct species. All three species bound the EGF receptor and stimulated the incorporation of tritiated thymidine into growth-arrested human fibroblasts. All of the forms are converted to a smaller biologically active form in the duodenum.

CONCLUSIONS

EGF exists in three distinct biologically active forms in normal rat milk. These forms are present at biologically relevant concentrations and are thought to participate in the growth and development of the newborn rat.

REPORT DATE: 03/08/91

WORK UNIT # 9276

DETAIL SUMMARY SHEET

TITLE: Internalization, Proteolytic Processing and Intracellular Trafficking of 125-I-Radiolabeled Epidermal Growth Factor (EGF) in Responsive and Nonresponsive Cell Lines

KEYWORDS: EGF, growth induction, processing

PRINCIPAL INVESTIGATOR: Schaudies, Paul CPT MS

DEPARTMENT: Department of Clinical Investigation

STATUS: Completed

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 8,841 Total: \$ 8,841

STUDY OBJECTIVE

To correlate cellular processing of epidermal growth factor (EGF) with the ability to regulate the growth response to EGF.

TECHNICAL APPROACH

Radiolabel epidermal growth factor and incubate with cultured cells. Monitor the progression of EGF within the cell, and examine the events stimulated by the growth factor.

PRIOR AND CURRENT PROGRESS

EGF binds the plasma membrane receptor and is processed into two additional forms subsequent to internalization. Inhibitors of acidification of the receptosome and lysosome inhibit the growth stimulus of EGF. These agents also inhibit the proteolytic processing of EGF which occurs within the endosome. When processing is inhibited by agents which neutralize the receptosome, intact and partially processed EGF are released from the cells into the media.

CONCLUSIONS

The pH change in the endosome is necessary for complete processing of the bound EGF. Inhibition of this process results in altered intracellular trafficking of the endosomal compartment.

REPORT DATE: 06/05/91

WORK UNIT # 9278

DETAIL SUMMARY SHEET

TITLE: Analysis of Amino Acids in Physiological Samples by High Pressure
Liquid Chromatography Using Ultrafiltration Technique

KEYWORDS: amino acid

PRINCIPAL INVESTIGATOR: Abdelrahim, Maged DAC

DEPARTMENT: Department of Clinical Investigation

STATUS: Completed
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 4,199 Previous FYs: \$ 8,526 Total: \$ 12,725

STUDY OBJECTIVE

To establish new reference values for amino acid analysis by using ultrafiltration technique instead of the current application of organic extraction technique.

TECHNICAL APPROACH

Use of high performance liquid chromatography, ultrafiltration technique, and Ortho-Phethaldehyde (OPA) pre-column derivatization.

PRIOR AND CURRENT PROGRESS

The study shows that recovery is 20% higher using the ultrafiltration technique over organic extraction without any loss in accuracy and reproducibility. The ultrafiltration technique reduced the sample preparation time from four samples per hour (using organic extraction) to 100 samples per 45 minutes.

CONCLUSIONS

The study has been completed, and the results are being analyzed and prepared for publication.

REPORT DATE: 09/16/91

WORK UNIT # 9279

DETAIL SUMMARY SHEET

TITLE: Clinical Competencies in Pediatric Physical Therapy: A Nationwide Survey of Practice

KEYWORDS: physical therapy, pediatric, competencies

PRINCIPAL INVESTIGATOR: Sweeney, Jane COL SP

DEPARTMENT: Department of Clinical Investigation

STATUS: Completed

APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

A national survey on the scope of practice and clinical competencies in pediatric physical therapy (PT) was established: a) to analyze pediatric PT practice in the United States and provide a structure for content areas for the Board examination in Pediatrics (PT), b) to compare results to the 1979 survey; and c) to describe demographic clinical practice characteristics of pediatric PT's in three professional associations.

TECHNICAL APPROACH

A questionnaire was mailed to the total membership of physical therapists in: a) Section on Pediatrics, American Physical Therapy Association; b) American Academy for Cerebral Palsy and Developmental Medicine; and c) Neurodevelopmental Treatment Association. A second questionnaire was mailed to all nonrespondents after 2 months.

PRIOR AND CURRENT PROGRESS

A 43% return rate of questionnaires occurred, yielding 1,900 questionnaires for analysis. Final results yielded a revalidation of all pediatric physical therapy competencies from the 1979 survey of practice. In addition, a new diagnostic/treatment category was identified: the medically fragile infant/child (technology dependent; organ transplant; infectious disease-HIV).

CONCLUSIONS

The developmental tests, diagnoses, and physical therapy procedures scored as "advanced level" by over 50% of the respondents will provide the basis for items written for the Board examination in Pediatric Physical Therapy, administered by the American Board of Physical Therapy Specialties.

REPORT DATE: 04/24/91

WORK UNIT # 9280

DETAIL SUMMARY SHEET

TITLE: Sleep and Respiratory Control i.. Kyphoscoliosis

KEYWORDS: sleep, kyphoscoliosis, nocturnal oxygenation

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

ASSOCIATES: Rajagopal, Krishnan LTC MC; Phillips, Yancy LTC MC

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 2,535 Previous FYs: \$ 0 Total: \$ 2,535

STUDY OBJECTIVE

To describe the hypercapnic and hypoxic rebreathing responses in kyphoscoliosis and to correlate these respiratory changes with the severity of the spinal deformity, as well as the frequency and severity of nocturnal oxygen desaturations as assessed by standard nocturnal polysomnography.

TECHNICAL APPROACH

Patients will be selected using Cobb's Angle to determine the severity of kyphoscoliosis as mild, moderate, or severe. In addition, patients must be 18 to 60 years old, FEV1/FVC > .07 predicted, absent of other conditions that might impair pulmonary function, and absent of medication that might affect respiration. Participants will be administered tests of full pulmonary function, arterial blood gases, comprehensive rebreathing under hypoxic and hypercapnic conditions, and nocturnal polysomnography.

PRIOR AND CURRENT PROGRESS

To date, no patients have been evaluated. The required instrumentation is in the final stages of development and should be fully functional no later than mid summer. Procedures for subject recruitment are in place and all investigators are aware of the current status of this protocol.

CONCLUSIONS

None at this time.

REPORT DATE: 09/11/91

WORK UNIT # 9281

DETAIL SUMMARY SHEET

TITLE: Relationship of Aryl Hydrocarbon Hydroxylase Activity to V-Beta T Cell Receptor Phenotype in Inbred Mouse Strains: A Model for Cancer Risk

KEYWORDS: V-beta T cell receptor, AHH, mls phenotype

PRINCIPAL INVESTIGATOR: Lippert, Lloyd PhD

DEPARTMENT: Department of Clinical Investigation

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 2,253 Previous FYs: \$ 0 Total: \$ 2,253

STUDY OBJECTIVE

To examine the T cell receptor (TCR) V-beta phenotype of inbred mouse strains and to determine it's relationship to inducibility of the P450 enzyme aryl hydrocarbon hydroxylase (AHH) activity.

TECHNICAL APPROACH

Restriction fragment length polymorphism (RFLP) analysis will be performed on DNA extracted from inbred mice spleen cells. The DNA will be digested with several restriction enzymes, Southern blotted, and probed with V-beta 6, 8.1 and 9 gene probes.

PRIOR AND CURRENT PROGRESS

Spleen cells from 14 different inbred mice strains have been used to extract DNA. The DNA has been digested with five restriction endonucleases and Southern blotted onto 15 nylon membranes. These membranes have been hybridized with three V-beta TCR genes, and more than 275 restriction fragments have been generated.

CONCLUSIONS

The comparison of presence or absence of any of the V-beta TCR genes to that predicted by mls phenotypes of the various mice strains is still to be analyzed. Also to be analyzed is the relationship between AHH inducibility and TCR V-beta phenotype.

REPORT DATE: 10/16/91

WORK UNIT # 8300

DETAIL SUMMARY SHEET

TITLE: Comparison of Psyllium Plantago and Xanthan Gum in the Dietary Management of Diabetes Mellitus

KEYWORDS: psyllium, xanthan gum, diabetes

PRINCIPAL INVESTIGATOR: Cowsar, John MAJ MC

SERVICE: DeWitt Army Community Hospital, Fort Belvoir, VA STATUS: Completed
APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To demonstrate that feeding psyllium plantago mucilage and xanthan gum can effectively improve glucose intolerance in patients with non-insulin dependent diabetes, and to examine the effect of these viscous fiber analogues on fasting insulin levels, serum total cholesterol, LDL, and triglycerides after the 6 week test period.

TECHNICAL APPROACH

Psyllium plantago mucilage (12 gm/day) and xanthan gum (12 gm/day) will be fed in gelatin capsules for 6 week intervals in a single blind, placebo cross-over design to human subjects. Forty-eight adult subjects with non-insulin dependent diabetes mellitus, having elevated fasting blood glucose within the range of 135-250 mg/dl, will comprise the test group. The test subjects will serve as their own controls. Fasting and 2 hour post 75 gm oral glucose challenge serum glucose measurements and lipids will be obtained at the start of the study, and again at the end of the test and placebo periods.

PRIOR AND CURRENT PROGRESS

Nine subjects have completed the study at Fort Benning. We were unable to start the project at Fort Belvoir due to lack of pharmacy support (loss of pharmacy technicians) and inadequate ancillary support in the Family Practice Department. I was also unable to recruit another co-investigator to assist with the project after CPT John Jacocks left Fort Belvoir. Zero subjects enrolled last year; total enrollment is 12. There were no adverse reactions in any of the subjects.

CONCLUSIONS

No conclusions were made since an inadequate number of subjects completed the project.

REPORT DATE: 10/09/91

WORK UNIT # 8301

DETAIL SUMMARY SHEET

TITLE: Immunogenicity of a Conjugated Hemophilus Influenzae Type B Vaccine in a High Risk Geriatric Population

KEYWORDS: Hemophilus influenzae, geriatric, immunogenicity

PRINCIPAL INVESTIGATOR: Carr, Robert MAJ MC

SERVICE: DeWitt Army Community Hospital, Fort Belvoir, VA STATUS: Completed
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the immunogenicity of a conjugated Hemophilus influenzae type b (HIB) vaccine in an elderly population with several risk factors for HIB disease.

TECHNICAL APPROACH

A total of 50 subjects over the age of 65 years received a polyribosylribitol phosphate-diphtheria conjugate (PRP-D) vaccine. Pre- and one-month post vaccination serum samples will be obtained.

PRIOR AND CURRENT PROGRESS

Serum samples from 49 subjects were sent for determination of capsular antibody level by radioimmunoassay (RIA). Out of the 49 subjects, 48 demonstrated a twofold and 42 demonstrated greater than a tenfold rise in antibody titer, with a mean rise in titer of 117.83 mcg/ml ($p=0.0001$). No significant side effects were noted.

CONCLUSIONS

The PRP-D vaccine appears to have substantial immunogenicity in this high risk geriatric population. Further studies may define the efficacy of this vaccine in preventing HIB disease in the elderly.

REPORT DATE: 05/31/91

WORK UNIT # 1151

DETAIL SUMMARY SHEET

TITLE: Evaluation of Renal Function, Protein Excretion and the Urinary Sediment in Patients with Antibody to the Human Immunodeficiency Virus (HIV)

KEYWORDS: urinalysis, kidney, HIV

PRINCIPAL INVESTIGATOR: Link, Christine CPT MC
ASSOCIATES: Moore, Jack LTC MC; Baker, James MAJ MC

SERVICE: HIV Research

STATUS: Completed
APPROVAL DATE: Mar 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To describe the renal function, protein excretion, and urinary sediment in patients positive to HIV antibody; and to determine if any abnormalities found are related to the severity of disease.

TECHNICAL APPROACH

After informed consent, three urine samples will be obtained. These will be used to examine the urinary sediment and to determine ability to acidify and concentrate urine after overnight fast. A 24-hour collection will be used to determine creatine clearance, total protein, and microalbuminuria. There has been no modification of the original protocol.

PRIOR AND CURRENT PROGRESS

Between April 1987 and May 1988, 59 patients were entered into the study. No patients have been withdrawn, there have been no adverse reactions, and the majority of patients have completed all portions of the study. A manuscript is being completed. No further patients are being entered into the study.

CONCLUSIONS

No patients had significant proteinuria or renal insufficiency, although abnormalities on urinalysis were not uncommon. There was no relationship between the severity of HIV disease and frequency of abnormalities.

REPORT DATE: 04/08/91

WORK UNIT # 1952

DETAIL SUMMARY SHEET

TITLE: The Clinical Presentation of HIV Infected Patients at Walter Reed Army Medical Center

KEYWORDS: HIV, epidemiology, disease progression

PRINCIPAL INVESTIGATOR: Oster, Charles COL MC

ASSOCIATES: Rhoads, Joanne MAJ MC; Birx, Deborah MAJ MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Jan 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate clinical and laboratory data on the first 402 adults seen in clinic at WRAMC who are infected with HIV-I by retrospectively reviewing their records.

TECHNICAL APPROACH

Chart review of medical records and laboratory studies on HIV infected patients.

PRIOR AND CURRENT PROGRESS

There has been no activity on this protocol, pending development of the computerized HIV Data Base.

CONCLUSIONS

There has been no activity; the data collection will begin after the HIV Data Base is set up, and medical records will be retrospectively reviewed at that time. The protocol should remain open and ongoing.

REPORT DATE: 03/29/91

WORK UNIT # 1953

DETAIL SUMMARY SHEET

TITLE: The Generation of Human Monoclonal Antibodies to the HIV

KEYWORDS: monoclonal, HIV, human

PRINCIPAL INVESTIGATOR: Drabick, Joseph CPT MC

ASSOCIATES: Baker, James MAJ MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Jan 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The purpose of this study is to generate human monoclonal antibodies to commercially available recombinant HIV antigen from the lymphocytes of patients infected with HIV.

TECHNICAL APPROACH

B. lymphocytes from peripheral blood or available lymphoid tissues are separated, then transformed with EBV. The transformed lymphocytes are screened for antibodies to HIV, recombinant HIV antigens, and recombinant soluble CD4. Positive wells are fused to heteromyeloma SHM-D33-0 and screened for specific antibody production. We are currently experimenting with MAB production from EBV transformed B cells without fusion. Likewise, we are developing a system to extract mRNA from EBV transformed B cells and transfect other cell lines for better MAB production.

PRIOR AND CURRENT PROGRESS

We have had good success in producing EBV transformed B cells from the peripheral blood of HIV infected patients, which produce antibodies to envelope and core proteins positive by WB and ELISA. The problem has been with scale-up to produce large amounts of the MAB's for experiments. We are purchasing a continuous perfusion bioreactor and hope to seed this with the EBV transformed B cells. This device can theoretically produce grams of pure MAB. Because of our changes in methodology we have kept our use of the protocol to a minimum but would like to begin acquiring blood again from protocol participants in the near future.

CONCLUSIONS

A human MAB against viral envelope may be useful in the prophylaxis of HIV infection (needle sticks and pre/perinatal use). Efforts to develop such a MAB are warranted because a prophylactic agent is of special interest to the military.

REPORT DATE: 08/07/91

WORK UNIT # 1958

DETAIL SUMMARY SHEET

TITLE: In Situ Hybridization for Detection of HIV in Langerhans Cells of HIV Infected Patients

KEYWORDS: HIV, Langerhans cells, macrophages

PRINCIPAL INVESTIGATOR: Hoover, David LTC MC
ASSOCIATES: Kalter, Chester MD

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine whether HIV genome is present in Langerhans cells of the skin; and b) to correlate percentage of infected Langerhans cells with degree of immunosuppression related to HIV infection and with infection on blood monocytes.

TECHNICAL APPROACH

Samples of normal skin will be examined by in situ hybridization for HIV and immunohistochemical methods to mark Langerhans cells (LC's). The percentage of HIV-infected Langerhans cells will be correlated with clinical stage as determined by the Walter Reed staging system.

PRIOR AND CURRENT PROGRESS

Skin biopsies, shave excisions, and suction blisters were obtained from 28 HIV-positive individuals and 5 controls. LC's were identified, studied morphologically, and enumerated by stains for HLA-DR and CD1 (#6). Skin was also stained with mAb to HIV-1, and compared to known positive control cells. In situ hybridization was performed on skin for HIV-1 mRNA. DNA-PCR for HIV Ltr/gag was performed on both skin sections and epidermal sheets. Skin samples were cocultured with target HIV-negative monocytes. Electron microscopy was also performed on skin samples.

CONCLUSIONS

Langerhans cell number was within normal range in HIV-positive patients, regardless of stage of disease. HIV-1 was readily detected in dermal skin samples, but rarely from epidermal only samples. We cannot support previously published views that LC's are an important reservoir of HIV-1.

REPORT DATE: 08/21/91

WORK UNIT # 3342

DETAIL SUMMARY SHEET

TITLE: Delayed Type Hypersensitivity Skin Testing: Correlation of Intradermal Injection Vs. Epicutaneous Antigen Placement and CD4 Number in Normals and HIV Seropositive Subjects

KEYWORDS: DTH, skin testing, multitest

PRINCIPAL INVESTIGATOR: Birx, Deborah MAJ MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Correlate antigen reactivity by intradermal and epicutaneous injection to circ. CD4 number. Compare subject reactivity to each of the antigens: tetanus, candida, trichophyton IC/multitest correlate anergy by multitest, and ID injection with evidence of HIV disease progression. Develop a standardized anergy panel to clinical staging of HIV infected patients.

TECHNICAL APPROACH

Simultaneous application of the multitest and ID injection of antigens in HIV infected patients.

PRIOR AND CURRENT PROGRESS

Progress of study was initially limited due to limited resources for patient accrual through Infectious Disease. Consequently, an efficient mechanism has been established with Dr. Oster's approval whereby patients are enrolled directly in the Allergy Clinic. Eighty-two patients have been enrolled; a total of 250 are needed for statistical significance through Stage VI. No significant adverse events have occurred; no volunteers have disenrolled from the study for these reasons.

CONCLUSIONS

A preliminary evaluation has shown that the primary difficulty with Multitest is the high reactivity on the control glycerine antigen in the HIV patients.

DETAIL SUMMARY SHEET

TITLE: Pathological Manifestations of HIV Infections at Autopsy

KEYWORDS: cause of death, histology, microbiology

PRINCIPAL INVESTIGATOR: Anderson, David MAJ MC

ASSOCIATES: Clark, Gary COL MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To 1) perform complete research autopsies on deceased patients with HIV disease, 2) document disease processes causing morbidity and mortality in patients enrolled in WRAMC HIV research, 3) obtain fresh tissue for immuno-histochemical detection phenotyping of immune cells and detection of viral infections, 4) obtain fresh tissue from major organ systems to store in a tissue registry: unfixed at -70 C and formalin-fixed, paraffin-embedded.

TECHNICAL APPROACH

Complete autopsies will be performed as soon after death as a valid research autopsy permit is available. Tissues from all major organ systems will be examined and processed for histochemistry (formalin-fixed, paraffin-embedded) or flash frozen for immune cell phenotyping. Routine histochemistry, special stains, and immune cell phenotyping will be performed, as well as microbiologic culture. Results will be assembled into a research autopsy protocol report which will be returned to the Infectious Disease Service, the deceased patient's chart, and the Jackson Foundation data base.

PRIOR AND CURRENT PROGRESS

WRAMC's autopsy rate for patients dying with HIV disease has increased from 38% (5/13) in the 13 mos ending Jan 89, to 60% (9/15) in the 12 mos Nov 89 and Nov 90. Causes of death: cardiomyopathy-2, pancreatitis-1, pneumonia-2, Kaposi's sarcoma-2, septicemia-2. A registry of fresh frozen tissues from major organ systems exists for all nine cases. The morgue's special autopsy suite has been renovated to permit full biohazard autopsies; and two labs in Anatomic Pathology Svc have been equipped to perform special stains, immune cell phenotyping, and microbiological assessment of tissues. Standardization of quantitative assessment of immune cell distribution within tissues through the use of computer-assisted light microscopic morphometry has begun. Mycobacterium avium-intracellulare was isolated from 8/9 cases. Group B, beta-hemolytic streptococcus was isolated from lungs of three autopsies.

CONCLUSIONS

WRAMC autopsy rate of HIV deceased patients can be increased even further. Infectious diseases continue to cause the majority of HIV-associated mortality. Cardiomyopathy and acute pancreatitis are important considerations in terminal course of HIV patients. The capability for systematic routine and frozen section processing of research autopsy tissues is now established.

REPORT DATE: 06/04/91

WORK UNIT # 6218

DETAIL SUMMARY SHEET

TITLE: Evaluation of Human Immunodeficiency Virus Related Proteins on the Surface of Lymphocytes from Children with Evidence of HIV Exposure or HIV Illnesses

KEYWORDS: flow cytometry, HIV antigen, mononuclear cell

PRINCIPAL INVESTIGATOR: Fischer, Gerald COL MC

ASSOCIATES: Baker, James MAJ MC; Zawadsky, Peter COL MC

SERVICE: HIV Research

STATUS: Completed

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The purpose of this study is to examine the presence of HIV antigen on different mononuclear cell populations in infants and children to evaluate its use in determining in vivo distribution of HIV in various cell lineages.

TECHNICAL APPROACH

Mononuclear cells are harvested from 1cc to 3cc of heparinized whole blood using standard methods. The mononuclear fraction is diluted to 10⁷ cells, and paired aliquots are incubated with anti-leu 3a PE, anti-leu 4 PE, and in selected case anti-leu M3 PE. These paired samples are then incubated with murine monoclonal anti-GP120 or anti-P24 and goat anti-murine IgG FITC. The samples and control specimens are then analyzed using FACS analysis.

PRIOR AND CURRENT PROGRESS

Preliminary data and conclusions were presented at the V International Conference on AIDS, Montreal, Canada, in June 1989. A total of 46 patients have been enrolled. A series of quality control experiments were conducted to verify the specificity of the findings. Patient enrollment has ceased pending review of the data developed to date and comparison to other techniques used to determine distribution and quantity of HIV in various cell lineages. While the technique was not suitable for use as a diagnostic assay, these studies did identify that in young infants (infected 2 degrees to maternal HIV infection) the peripheral blood macrophage was the major secondary cell type infected with HIV.

CONCLUSIONS

The technique evaluated in this study, based on preliminary data, has shown a relationship between disease stage and the ability to identify cell-associated HIV antigen. However, the technique is labor intensive and may not have any advantage over others currently under development for diagnosis. However, it may be useful to study HIV infection of specific cell types.

REPORT DATE: 08/29/91

WORK UNIT # 6220

DETAIL SUMMARY SHEET

TITLE: Epidemiology of HIV In Pediatric and Perinatal Patients - A Natural History Study

KEYWORDS: immunodeficiency, pediatric, epidemiology

PRINCIPAL INVESTIGATOR: Fischer, Gerald COL MC

ASSOCIATES: Pettett, Gary COL MC; Scott, Robert COL MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The purpose of this study is to develop a Military Pediatric HIV Program for identification of military dependents (spouses and children) of HIV infected personnel. The study will identify basic epidemiologic information and follow these high risk or HIV-infected children over time to assess infection status and disease progression.

TECHNICAL APPROACH

The Military Pediatric HIV Program will identify children at high risk for HIV infection by matching USAHDS reports with the computer linked DEERS data files. All families with one or both spouses infected with HIV will be offered voluntary enrollment in this program. In addition, children with illness or other problems associated with HIV infection may also be voluntarily enrolled in this study. All children followed will be periodically reevaluated using state-of-the-art HIV diagnostic tests. It is anticipated that this program will encompass Army, Air Force, and Navy dependents.

PRIOR AND CURRENT PROGRESS

Over the last year, programs have been established for all military dependents throughout the country. There were patients on protocol at WRAMC (73), National Naval Medical Center (23), San Diego Naval (17), and Wilford Hall Air Force Medical Center (13); for a total of 126. As we follow these children prospectively, several important findings have emerged: 1) infected children fall into two categories, those who become ill and develop AIDS in the first few months of life and those who are infected but asymptomatic for several years (slow progressors); 2) most HIV positive mothers in our population are asymptomatic (WR Stage 1 or 2), and 3) the military perinatal HIV transmission rate is very low (less than 10%).

CONCLUSIONS

Prospective evaluation of HIV infected women and their offspring, and HIV infected or high-risk children, will provide important information on the transmission and progression of HIV infection in women and children.

REPORT DATE: 08/29/91

WORK UNIT # 6222

DETAIL SUMMARY SHEET

TITLE: Core Project: Evaluation of Diagnostic Assays for Human
Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure
or HIV Illnesses

KEYWORDS: AIDS, diagnosis, cultures

PRINCIPAL INVESTIGATOR: Fischer, Gerald COL MC
ASSOCIATES: Burke, Donald COL MC; Ascher, David MAJ MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

- a) To analyze laboratory assays for detection of HIV infection in children; and
- b) To correlate the results with the clinical status of the child.

TECHNICAL APPROACH

This protocol will evaluate the usefulness of new diagnostic assays for HIV as they are developed using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard ("state-of-the-art") HIV testing (generally those tests that are most developed). The surplus will be utilized for less well developed assays or stored for future analysis. Results from all tests will be compared to conventional assays used to diagnose adult HIV infection (ELISA, Western Blot) to determine their usefulness in children.

PRIOR AND CURRENT PROGRESS

Over the last year, HIV cultures have continued to be analyzed in comparison with Western Blot (WB) and polymerase chain reaction (PCR). Cultures and PCR are consistently positive in infants at a time when WB is nondiagnostic for HIV infection (3-9 months). In addition, cultures and PCR continue to show greater than 95% sensitivity and specificity. Rapid time to positive culture and plasma viremia continue to be associated with advanced disease stage.

CONCLUSIONS

HIV cultures and PCR are exceedingly important tests for diagnosis of HIV infection in children, especially young infants. These studies need to be continued to further evaluate these diagnostic tests and their prognostic value.

REPORT DATE: 06/27/91

WORK UNIT # 6264

DETAIL SUMMARY SHEET

TITLE: Perinatal HIV Infection: Epidemiology and Natural History

KEYWORDS: natural history, perinatal HIV, epidemiology

PRINCIPAL INVESTIGATOR: Pettett, Gary COL MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To develop a central perinatal program for the identification, evaluation, and follow-up of HIV-infected pregnant women and their newborn infants, and to describe the clinicopathologic correlates most predictive of perinatal transmission of HIV.

TECHNICAL APPROACH

High risk pregnant women and maternal-infant pairs are prospectively entered into a longitudinal study to evaluate immunologic status and detect vertical transmission of HIV infection in early infancy. Quarterly clinical examination and serologic/immunologic assays are utilized to fully characterize the immune status of all patients. Statistical analysis of clinical and laboratory results will be directed toward the identification of perinatal factors which are reliable predictors of vertical transmission.

PRIOR AND CURRENT PROGRESS

Since this protocol was approved, a total of six maternal-infant pairs have been enrolled. The majority of women have been in the early stages of HIV infection (Walter Reed Stage 1-3) and have had intact immune systems. Follow-up has ranged from 2-13 months. Vertical transmission has occurred in only one pair (16.7%). Diagnosis of HIV infection (vertical transmission) was made at 3 months of age. Despite the early appearance of HIV infection, this infant's disease has not yet progressed to a more serious immunodeficiency (current age 13 months).

CONCLUSIONS

The study population is presently too small to support any significant conclusions. However, it is apparent that without the close follow-up in the one transmitting pair, a diagnosis of HIV infection would not have been made from clinical symptoms alone. Our preliminary experience supports the need for more frequent evaluations of high-risk patients to detect HIV infection in young infants as early as possible.

REPORT DATE: 04/01/91

WORK UNIT # 7128

DETAIL SUMMARY SHEET

TITLE: Neurobehavioral Consequences of HTLV-III Brain Infection and AIDS
Encephalopathy

KEYWORDS: HIV, AIDS, neurobehavior

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: HIV Research

STATUS: Completed

APPROVAL DATE: Dec 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the natural history of neurologic and behavioral effects of HIV infection.

TECHNICAL APPROACH

Initial and six month follow-up multidisciplinary evaluation of Stage I, II, and III patients.

PRIOR AND CURRENT PROGRESS

The neurological and cognitive manifestations of early HIV infection have been prospectively characterized with multiple examinations on 95 HIV patients and 90 HIV negative controls. A screening instrument to detect the early onset of neurobehavioral changes in HIV infection has been developed and successfully tested in 95 HIV patients and 90 controls. Host, virus, infection, and epidemiologic factors affecting these manifestations and their progression have been investigated, and two neurotoxins have been identified in early HIV CSF. One of these correlates highly with cognitive deficits in information processing. A structure for the systematic testing and evaluation of HIV patients in drug trials has been established and successfully tested in one drug trial.

CONCLUSIONS

HIV infection in its earliest stages (WR 1-3) causes subtle but clearly defined clinical deficits in information processing and procedural learning correlating strongly with quinolinic acid (an NMDA receptor excitotoxin) elevations in the CSF. These deficits are not seen in HIV negative asymptomatic or depressed control patients. The quinolinic acid elevations appear to be related to interferon abnormalities - about 50% of patients had a gp120-like neurotoxin in their CSF.

REPORT DATE: 07/17/91

WORK UNIT # 7139

DETAIL SUMMARY SHEET

TITLE: Intramuscular Poly-ICLC and Zidovudine in the Management of HIV
Infection: An Open Pilot Trial

KEYWORDS: poly-ICLC, zidovudine, HIV

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: HIV Research

STATUS: Completed

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the safety or toxicity of poly-ICLC plus zidovudine in patients with advanced HIV infection based on historical controls. To study the human response to poly-ICLC plus zidovudine in patients with AIDS. To explore zidovudine in the management of HIV infection, based on historical controls.

TECHNICAL APPROACH

Poly-ICLC (5,10,50 or 100 mcgm/kg) is administered IM one to four times a month. Clinical, laboratory, and immunological parameters are followed.

PRIOR AND CURRENT PROGRESS

Eleven (11) patients were entered into the study; two dropped out, and two were removed for technical reasons. Eight (8) patients remained on study long enough for analysis. Patients have generally tolerated medication well. There has been no unexpected change in T-cell subsets or incidence of opportunistic infection, although performance on reaction time tests improved during drug administration.

CONCLUSIONS

Poly-ICLC can be safely administered to AIDS patients. The optimum dose from a clinical tolerance point of view is likely to be in the 10-20 mcgm/kg range, two to three times per week. Further studies are required to evaluate efficacy.

REPORT DATE: 06/13/91

WORK UNIT # 7243

DETAIL SUMMARY SHEET

TITLE: Psychiatric Natural History Study: Factors Related to Human Immunodeficiency Virus Transmission and Morbidity

KEYWORDS: HIV risk behaviors, early HIV disease, military performance

PRINCIPAL INVESTIGATOR: Rundell, James MAJ MC

ASSOCIATES: Nannis, Ellen PhD; Brandt, Ursula PhD

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine potential areas for effective interventions designed to reduce HIV transmission by HIV-infected military medical beneficiaries, and to reduce neuropsychiatric complications of HIV disease progression in infected military medical beneficiaries.

TECHNICAL APPROACH

Military medical beneficiaries from all three services (500 from Walter Reed Army Medical Center, 700 from Wilford Hall, 300 from National Naval Medical Center, and 400 from San Diego Naval Hospital) will be asked to complete anonymous risk behavior assessments. Smaller numbers of infected individuals are recruited to participate in other non-anonymous protocol core areas; psychosocial (N=1,400), psychiatry (N=1,000), stress and coping (N=1,000), and neuropsychology (N=500). These non-anonymous but confidential portions of the protocol will be repeated at each patient's routine medical re-evaluation.

PRIOR AND CURRENT PROGRESS

The protocol began enrolling patients shortly after final approval. To date, 200 patients have been enrolled at Walter Reed, 450 at Wilford Hall, 200 at San Diego Naval Hospital, and none at National Naval Medical Center (final approval by NNMCM is anticipated soon). Subject enrollment will be completed, and first wave data will be analyzed and reported. The protocol team will then focus on collecting longitudinal data and writing secondary protocols that capitalize on areas suggested as potential areas for effective interventions.

CONCLUSIONS

Protocol enrollment at Wilford Hall is ahead of projections and is equal to projected numbers at Walter Reed and San Diego Naval Hospital. National Naval Medical Center's final approval is anticipated by mid-summer 1991. No difficulties in accomplishing aims and objectives of RV-26 are anticipated.

REPORT DATE: 03/12/91

WORK UNIT # 8801

DETAIL SUMMARY SHEET

TITLE: Identification and Characterization of Human Immunodeficiency Virus in Human Semen

KEYWORDS: HIV, semen

PRINCIPAL INVESTIGATOR: Rhoads, Joanne MAJ MC

SERVICE: HIV Research

STATUS: Completed
APPROVAL DATE: Mar 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To identify, through culture and antigen detection, HIV in human semen and to characterize the immune response to HIV in the seminal compartment.

TECHNICAL APPROACH

a) Culture of semen (cell and seminal plasma); b) Evaluation of seminal plasma for HIV antibodies with comparison to serum HIV antibodies (ELISA and Western Blot); c) Evaluation of HIV antigens in the seminal plasma (p24 ELISA).

PRIOR AND CURRENT PROGRESS

This study is closed. No further specimens have been collected since the last Annual Progress Report.

CONCLUSIONS

The data support the concept that the male reproductive tract is an immunologically privileged site, and HIV replication and control in this compartment may differ from the serum.

REPORT DATE: 06/14/91

WORK UNIT # 8802

DETAIL SUMMARY SHEET

TITLE: VA Cooperative Study No. 298, Treatment of AIDS and AIDS Related Complex; Part I: Treatment of Patients with ARC (AZT Vs. Placebo)

KEYWORDS: zidovudine, HIV, ARC

PRINCIPAL INVESTIGATOR: Oster, Charles COL MC

ASSOCIATES: Hawkes, Clifton MAJ MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Apr 1988

FUNDING: Current FY: \$ 996 Previous FYs: \$ 0 Total: \$ 996

STUDY OBJECTIVE

To determine the effectiveness of AZT (zidovudine) on AIDS Related Complex (ARC) - Walter Reed Stages 2-4.

TECHNICAL APPROACH

This is a randomized double-blind placebo-controlled study. Subjects who meet the inclusion criteria, after screening, are randomized onto the study drug. Half of the subjects receive AZT 250 mg every 4 hours, while the other half receive a placebo. In January 1991, Part I was completed; all participants were informed of their original treatment assignment and given the opportunity to remain or be started on open-label zidovudine or placebo. In March 1991, an addendum was approved which allowed for extended follow-up for all participants who agreed to continue and sign a revised informed consent (dated March 1991).

PRIOR AND CURRENT PROGRESS

The total enrollment at the time of completion of Part I was 20 subjects. To date, enrollment for Part II (extended follow-up) is four subjects. There have been no serious or unexpected adverse reactions, and no patients have withdrawn since last APR. Benefit to participants apply largely to those on zidovudine (early) who exhibited delayed progression to AIDS (WR Stage 6).

CONCLUSIONS

In symptomatic HIV-infected patients, early zidovudine therapy delayed progression to AIDS or WR Stage 6 but was associated with more side effects. It had no effect on survival. The long-term effects of zidovudine on quality of life, on cumulative drug toxicity, on development of drug resistance, and on costs of therapy have not been fully defined. Thus, one may consider delaying the initiation of zidovudine in stable patients with CD4 counts between 200-500 cells per mm³.

REPORT DATE: 05/04/91

WORK UNIT # 8803

DETAIL SUMMARY SHEET

TITLE: Core Protocol for HIV Developmental Diagnostics (Adults)

KEYWORDS: HIV, AIDS, virus culture

PRINCIPAL INVESTIGATOR: Roberts, Chester, LTC MS

ASSOCIATES: Oster, Charles COL MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To develop and evaluate new and/or improved laboratory methods for establishing the diagnosis of HIV infection and for determining the stage of illness.

TECHNICAL APPROACH

Methods to detect replicating HIV virus, HIV antigens, and HIV nucleic acids are used, including, for example, virus culture, antigen capture immunoassay, and polymerase chain reaction (PCR) amplification of HIV DNA.

PRIOR AND CURRENT PROGRESS

From April 1991 through May 1991, 292 blood specimens were collected and analyzed. These generated 600 co-cultures and 462 polymerase chain reactions. In addition, 46 of the above samples were also tested for serum p24 antigen which generated 128 determinations through serum dilutions. Other diagnostic tests performed include radioimmunoprecipitation assays (RIPA's) and mitogen proliferative response assays.

CONCLUSIONS

HIV-1 detection by culture and PCR are extremely sensitive techniques and can be offered as routine clinical tests. Through these techniques the "window" between infection and detection of that infection has been narrowed considerably.

REPORT DATE: 06/11/91

WORK UNIT # 8804

DETAIL SUMMARY SHEET

TITLE: The Natural History of HIV Infection and Disease in United States
Military Beneficiaries

KEYWORDS: HIV, natural history, AIDS

PRINCIPAL INVESTIGATOR: Oster, Charles COL MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To systematically document the natural disease progression of HIV infection.

TECHNICAL APPROACH

Information, already being routinely collected on HIV patients, is being organized into a data base in such a way that more scientifically valid information will be forthcoming. Safeguards to patient confidentiality are met. This data base forms the core around which other specific protocols can be built.

PRIOR AND CURRENT PROGRESS

From June 1990 to May 1991, the Infectious Disease Clinic at WRAMC followed 601 patients. As of June 1991, 516 patients are enrolled in this protocol. Ninety-nine patients were enrolled in the last year. There were two dropouts. Natural history data continues to be collected.

CONCLUSIONS

The data from this protocol is still being collected. There are no conclusions at this time.

REPORT DATE: 03/26/91

WORK UNIT # 8805

DETAIL SUMMARY SHEET

TITLE: Natural History of Oral Manifestations of HIV Infection in a United States Military Population

KEYWORDS: epidemiology, oral diseases, HIV

PRINCIPAL INVESTIGATOR: Tramont, Edmund COL MC

ASSOCIATES: Swango, P CAPT USN; Kleinman, D CAPT USN

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To document the prevalence and incidence of oral manifestations of HIV infection in relation to the degree of immunodeficiency. Emphasis is given to oral pathologies, periodontal disease, oral candidal infections, and the effect of HIV on salivary constituents.

TECHNICAL APPROACH

Volunteers receive a comprehensive oral examination at entry and every six months thereafter. This evaluation includes clinical examinations for dental caries, periodontal disease, and oral mucosal pathologies. Dental plaque and saliva samples are collected for microbial and biochemical assays, and a questionnaire on oral health-related behaviors and history is administered. Data are analyzed in relation to subjects' medical condition and immune status.

PRIOR AND CURRENT PROGRESS

One hundred and thirty-six subjects were enrolled during the past year, bringing the current total to 514. Of these, 366 have received their initial baseline oral examination, and 167 have also received at least one 6-month follow-up exam. No adverse reactions have been reported, and no patients have withdrawn from the study. Benefits to subjects include early diagnosis of oral disease, dental prophylaxis, limited emergency care, and referral for appropriate treatment.

CONCLUSIONS

Oral fungal and viral infections occurred in about 30% of subjects, and were strongly associated with T4 cell counts and Walter Reed Stage. Oral candidiasis was present in 16% and was associated with current tobacco use. Periodontal destruction was prevalent, but its relation to degree of immune dysfunction remains unclear. Prevalence of mucosal pathologies increased significantly within a 6-month follow-up period.

REPORT DATE: 03/15/91

WORK UNIT # 8806

DETAIL SUMMARY SHEET

TITLE: Active Immunization of HIV Infected Patients with Recombinant GP160 HIV Protein: Phase I Study of Immunotherapy, Immunogenicity and Toxicity

KEYWORDS: HIV infection, immunotherapy, gp160

PRINCIPAL INVESTIGATOR: Redfield, Robert LTC MC

ASSOCIATES: Birx, Deborah MAJ MC; Davis, Charles LTC MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the immunogenicity and toxicity of recombinant expressed gp160 in patients with early HIV infection.

TECHNICAL APPROACH

This is a Phase I immunogenicity and toxicity trial consisting of six groups of five patients each to receive recombinant expressed gp160 vaccine as an active immunization at increasing doses ranging from 40ug to 640ug, and by two distinct vaccine schedules: 0, 30, 120 vs 0, 30, 60, 120, 150, 180 days. Alterations in cellular and humoral immune response to HIV specific proteins will be assessed as well as alterations in in vivo and in vitro cellular immune function.

PRIOR AND CURRENT PROGRESS

Nineteen of 30 HIV infected volunteers increased both humoral and cellular anti-HIV envelope immunity in response to gp160 vaccination. Seroconversion to selected envelope epitopes, and new T cell proliferative responses to gp160 were seen. Responsiveness to vaccination increased with number given; 87% of volunteers who received six injection regimen responded versus 40% of those randomized to three injections ($p=0.02$). No adverse systemic reactions were seen. Local reactogenicity at the site of injection was mild. No diminution of general in vitro or vivo cellular immune function was seen. After 10 months of follow-up there was no decline in mean CD4 count for the 19 vaccine responders while CD4 counts among non-responders declined 7.3%. Volunteers randomized to six injections demonstrated net increase in mean CD4 cell counts, compared to a 7.2% decrease in volunteers receiving three injections. Study is closed to recruitment.

CONCLUSIONS

HIV specific vaccine therapy is feasible in the setting of chronic HIV infection. The use of this gp160 vaccine in volunteers with early HIV infection was safe and immunogenic. Volunteers with early HIV infection were capable of increasing their HIV specific immunity in response to vaccination.

REPORT DATE: 03/29/91

WORK UNIT # 8807

DETAIL SUMMARY SHEET

TITLE: The Use of Cimetidine for Immunoaugmentation in HIV Seropositive Patients

KEYWORDS: HIV, cimetidine, immunoaugmentation

PRINCIPAL INVESTIGATOR: Drabick, Joseph CPT MC

ASSOCIATES: Birx, Deborah MAJ MC; Oster, Charles COL MC

SERVICE: HIV Research

STATUS: Completed

APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if oral cimetidine has the ability to stimulate immune function in already immunodeficient HIV patients and, hence, be useful as an adjunctive therapy in the management of advanced HIV disease.

TECHNICAL APPROACH

In an open label prospective study, patients receive cimetidine in a dose known to cause immunoaugmentation. Immunologic parameters such as DHS, in vitro blastogenesis to standard mitogens and antigens, as well as HIV antigens, and cell counts are determined before, during, and after drug therapy. Virologic parameters such as viral culture and p24 antigen levels are also measured.

PRIOR AND CURRENT PROGRESS

The study is now complete, and data analysis has begun pending receipt of some remaining blastogenesis data. Seven patients were enrolled; two dropped out because of problems not related to the cimetidine which was well tolerated by all patients without hematologic side effects. There was a significant increase in DHS responses which was dependent on initial CD8 count ($p < .05$) and the magnitude was dependent on the CD8 count ($p < .05$). Patients with initial CD8 counts less than 900 did not respond. Only two patients were p24 positive, and in these, there was a decrease in levels, though not significant. All were culture positive without change. No change in CD4. CD8 or ratio was noted. Two responders felt clinically improved.

CONCLUSIONS

Cimetidine is safe and well tolerated in HIV pts. Significant increases in DHS were observed, and the presence and magnitude of the response was dependent on the initial CD8 count, suggesting benefit would be limited to only some HIV pts. No significant effects on virologic parameters were observed, though a trend to a decreased antigenemia was observed in responders. Although 2/3 responders felt clinically improved, the clinical correlate of improved DHS is uncertain.

DETAIL SUMMARY SHEET

TITLE: A Pharmacokinetic Study to Develop a Database to Describe the Relationship Between Zidovudine (AZT)/Glucuronyl (GAZT) Blood Levels and Drug Toxicity in HIV Infected Patients

KEYWORDS: pharmacokinetics, toxicity, zidovudine

PRINCIPAL INVESTIGATOR: Bjornson, Darrell LTC MS
ASSOCIATES: Lombardo, Fred MAJ MS; Park, Soon PhD

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define the relationship of zidovudine (ZDV) and glucuronyl zidovudine (GZDV) peak and through plasma blood levels with drug toxicity.

TECHNICAL APPROACH

Patients who are prescribed zidovudine for the first time have venous blood samples drawn each month for 12 months: 0, 15, 30, 45, 60, and 75 minutes. Levels of ZDV and GZDV are analyzed with the ZDV-Trac RIA kit, and concurrent toxicity parameters are followed. Multiple regression analysis is used to analyze data.

PRIOR AND CURRENT PROGRESS

Nineteen patients have been enrolled in the study, with 15 patients completing the 1 year pharmacokinetic portion. There have been no serious or unexpected adverse reactions. There has been no known benefit to the patients. Four patients are at month 8 of 12 in the pharmacokinetic portion of the study. Follow-up will continue on all patients beyond the 12 months. Final pharmacokinetic analysis will be done in approximately 8 months. Enrollment beyond 19 patients is not expected unless we can enroll one more female patient.

CONCLUSIONS

Interim analysis in December 1990 (15 patients) suggested an association between hemoglobin decline and peak metabolite (GZDV) levels and granulocyte decline in both peak GZDV and ZDV levels. The best predictor in each case was peak GZDV. There were wide inpatient variations in plasma concentrations from month to month and wide interpatient variations in plasma concentrations even when corrected for body weight.

REPORT DATE: 04/08/91

WORK UNIT # 8809

DETAIL SUMMARY SHEET

TITLE: Phase I and II Study of the Use of Soluble CD4 Protein (sCD4: St4 SK&F 106528) in Human Immunodeficiency Virus Infection

KEYWORDS: soluble, CD4, HIV

PRINCIPAL INVESTIGATOR: Hawkes, Clifton MAJ MC

ASSOCIATES: Sun, Wellington MAJ MC; Virani, Nzeera MD

SERVICE: HIV Research

STATUS: Completed

APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To assess the safety and tolerability of a single intravenous infusion of soluble CD4 in HIV-infected patients, Stages WR 3-5; and b) To evaluate the pharmacokinetics and bioavailability of soluble CD4 at the beginning of the study, during the course of the study, and at the end of the study.

TECHNICAL APPROACH

The Phase I study was an open, randomized, but unblinded trial. Subjects who met the inclusion criteria, after screening, were randomly assigned to one of three treatment arms using soluble CD4 at doses of 0.1, 0.3, or 1.0 mg/kg. There was no placebo group.

PRIOR AND CURRENT PROGRESS

The Phase I study was completed in 1989. A proposed Phase II study evaluating the efficacy of Soluble CD4 by continuous infusion was aborted because of technical difficulties, unavailability of study drug, as well as new information suggesting that Soluble CD4, as currently formulated, was not likely to be effective. No further studies with this drug are anticipated or planned at this time.

CONCLUSIONS

As reported last year, the results of the Phase I study showed that Soluble CD4 was well-tolerated with few side effects, and none which required termination of drug. No additional data is or will be available.

REPORT DATE: 05/14/91

WORK UNIT # 8810

DETAIL SUMMARY SHEET

TITLE: Factors Affecting Heterosexual Transmission of Human Immunodeficiency Virus

KEYWORDS: HIV, heterosexual, transmission

PRINCIPAL INVESTIGATOR: Rhoads, Joanne MAJ MC

ASSOCIATES: Levin, Lynn PhD

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the factors which determine the heterosexual venereal transmission of human immunodeficiency virus (HIV), in order to develop preventive and interventive therapies.

TECHNICAL APPROACH

This study is designed in two parts: a cross-sectional, case control study of concordant and discordant HIV infected couples, followed by a prospective study of the discordant pairs.

PRIOR AND CURRENT PROGRESS

No subjects have been enrolled, to date, into this study. An addendum to the original protocol is being submitted by a new PI, Lynn I. Levin, Ph.D., Department of Epidemiology, Walter Reed Army Institute of Research. Resolution regarding a new PI and enrollment of subjects should occur during the next reporting period.

CONCLUSIONS

None at this time.

REPORT DATE: 06/12/91

WORK UNIT # 8811

DETAIL SUMMARY SHEET

TITLE: The Investigation of the Cutaneous Microflora Found in HIV Infected Patients as it Relates to the Onset, Severity and Progression of Disease

KEYWORDS: cutaneous microflora, immunohistochemical stain

PRINCIPAL INVESTIGATOR: Smith, Kathleen LTC MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To document skin changes associated with HIV disease, both clinical and histopathologic, and to follow these changes with progression of disease, with emphasis on histopathologic studies to identify both clinical and subclinical infections. Immunohistochemical markers of the inflammatory infiltrate in HIV disease. Microbiologic studies of the cutaneous microflora, both in all stages and with progression of disease.

TECHNICAL APPROACH

(1) Cutaneous exam questionnaire and examination at initial visit. (2) Diagnostic biopsy with a battery of special stains to identify both clinical and subclinical infections and primary diagnosis. (3) Immunohistochemical studies of the inflammatory infiltrate. (4) Cultures of cutaneous microflora in seven designated areas; microbiology done by University of Pennsylvania.

PRIOR AND CURRENT PROGRESS

We have cultured 75 patients which is well over half the number of HIV+ patients necessary to complete the protocol and all of them matched controls. We have collected lipids from the forehead and cheek areas on all patients cultured. We are at present considering a possible treatment protocol to help control high levels of Staphylococcus aureus carriage,

CONCLUSIONS

We have found an increase in Staphylococcus aureus carriage early in the disease, which correlates with increasing xerosis.

REPORT DATE: 06/12/91

WORK UNIT # 8812

DETAIL SUMMARY SHEET

TITLE: The Investigation of the Cutaneous Manifestations of HIV Infection in Relation to the Onset, Severity and Progression of Disease, Dermatologic Natural History

KEYWORDS: HIV, dermatology

PRINCIPAL INVESTIGATOR: Smith, Kathleen LTC MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study cutaneous manifestations, both histologically and clinically, in relation to disease onset and progression of disease.

TECHNICAL APPROACH

A complete dermatology examination, including a complete history, is performed. Lesional biopsies (4-6 mm punch) are performed, as needed, for diagnosis. Lesional biopsies may be split and half frozen for performing immunohistochemical markers of the inflammatory infiltrate. In addition, special stains are performed to rule out infections. The patients are followed up every 6 months and may be seen for problems that develop between visits. In addition, seven cutaneous sites are cultured for fungus and bacteria in patients in all stages of disease; repeat cultures are performed if the stage changes.

PRIOR AND CURRENT PROGRESS

Over 450 patients are currently being seen in both the Bethesda and Walter Reed Protocol. Many patients have returned for their second follow-up visit, and several are being seen for their third visit. Approximately 300 biopsies have been evaluated by routine and special stains and by one battery of immunoperoxidase stain. This data has been entered, and a manuscript is in preparation. Immunoperoxidase staining has been started on the tissue that was frozen at the time of the biopsy.

CONCLUSIONS

We are gaining experience in the cutaneous manifestations seen throughout HIV disease and in treatment of these conditions. We have a large group of biopsies of inflammatory conditions with lymphoid markers throughout disease, as well as histologic patterns seen throughout the disease.

REPORT DATE: 08/14/91

WORK UNIT # 8814

DETAIL SUMMARY SHEET

TITLE: Pharmacoepidemiologic Study to Develop a Database to Document Variations in the Outcome of Illness Which May be Due to Drug Effects and To Document Patterns of Drug use in HIV Infected Patients

KEYWORDS: pharmacoepidemiology, data base, drug use

PRINCIPAL INVESTIGATOR: Bjornson, Darrel LTC MS

ASSOCIATES: Oster, Charles COL MC; Hiner, William COL MS

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To develop a data base to study outcomes of illness due to drug effects (both beneficial and adverse), and to gather useful information on drug use patterns of HIV infected patients.

TECHNICAL APPROACH

To develop a data base in conjunction with the Henry M. Jackson Foundation (HMJF) HIV data base which will allow for the retrospective and prospective collection and review of clinical data and prescription data on HIV infected patients.

PRIOR AND CURRENT PROGRESS

Currently, all patients on zidovudine and dideoxyinosine have been entered into the data base (a total of 216). The template for the HIV data base (HMJF) has been written, and prescription drug data is currently being entered by physician assistants.

CONCLUSIONS

No conclusions can be reached at this time. This is an ongoing study with long-term follow-up.

REPORT DATE: 09/14/91

WORK UNIT # 8815

DETAIL SUMMARY SHEET

TITLE: Pneumocystis Carinii Pneumonia in HIV Patients: A Cohort Study to Estimate the Protective Effect of Prophylactic Pentamidine Inhalation in Compliant Vs. Noncompliant Patients

KEYWORDS: PCP, HIV, compliance

PRINCIPAL INVESTIGATOR: Bjornson, Darrel LTC MS
ASSOCIATES: Oster, Charles COL MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if patients who are compliant with the use of pentamidine inhalation have a decreased risk of developing Pneumocystis carinii pneumonia (PCP) when compared to those who are noncompliant. In addition, we will look to see if there is a difference between monthly and twice monthly regimens regarding compliance.

TECHNICAL APPROACH

A cohort of patients were selected for the study who had been prescribed prophylactic pentamidine inhalation. Incidence of PCP will be collected from the medical records, with compliance data from the pharmacy records. Analysis will determine whether the risk of PCP is greater in patients who are noncompliant with pentamidine therapy versus those who are compliant. In addition, the 300 mg monthly dose will be compared with the 60 mg twice monthly dose regarding compliance.

PRIOR AND CURRENT PROGRESS

The compliance data for 186 patients (1988-1990) is now being collected and tabulated by the research pharmacy technician. Data on outcome events (PCP) was recently received from the U.S. Army Patient Administration Systems and Biostatistical Activity (PASBA) via Patient Administration Directorate, WRAMC. Data analysis and interpretation will be completed in 1991.

CONCLUSIONS

None. Data still being collected.

REPORT DATE: 03/26/91

WORK UNIT # 8817

DETAIL SUMMARY SHEET

TITLE: The Effect of HIV Infection on the Initial Manifestations and Response to Treatment of Syphilis

KEYWORDS: HIV, syphilis, treatment

PRINCIPAL INVESTIGATOR: Johnson, Steven MAJ MC

ASSOCIATES: Hicks, Charles LTC MC; Tramont, Edmund COL MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare current therapy of syphilis with a more intensive regimen in patients with and without HIV infection.

TECHNICAL APPROACH

Randomized double-blind placebo-controlled comparison of two antibiotic treatment regimens for HIV-infected patients with syphilis.

PRIOR AND CURRENT PROGRESS

This multicenter study began late January 1991. One patient has been enrolled at WRAMC, and two patients have been enrolled at National Naval Medical Center (NNMC).

CONCLUSIONS

No important findings have been reported this early in the study.

REPORT DATE: 04/03/91

WORK UNIT # 8818

DETAIL SUMMARY SHEET

TITLE: Prospective Study of the Emergence of Zidovudine Resistance in Patients Infected with the Human Immunodeficiency Virus who are Treated with Zidovudine

KEYWORDS: AZT resistance, virus culture, HIV

PRINCIPAL INVESTIGATOR: Mayers, Douglas CDR MC

ASSOCIATES: Oster, Charles COL MC; Wagner, Kenneth MD

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if there exists a level of AZT resistance, measured in vitro, which correlates with clinical deterioration in patients receiving AZT. Secondly, to determine the time course, frequency and clinical parameters associated with development of AZT resistance, and to develop a repository of HIV-infected PBMC and plasma for future studies of AZT resistance.

TECHNICAL APPROACH

HIV-infected patients taking AZT will be clinically evaluated every 3 months. Blood will be drawn at each evaluation for HIV-culture, p24Ag, T cell subsets, and AZT levels. Aliquots of PBMC and plasma will be stored in liquid nitrogen. HIV isolates will be evaluated for susceptibility to AZT, DDC, and DDL. Genotypic analysis of the HIV reverse transcriptase gene will be performed on selected patient isolates. Primary clinical endpoints are death or development of a new opportunistic infection. Data will be evaluated using a Mantel-Haenszel survival analysis with transition states.

PRIOR AND CURRENT PROGRESS

Ninety-one patients have been enrolled at WRAMC and the National Naval Medical Center since the study was initiated in October 1990. Enrollment of 100 active patients should be completed by September 1991. Patients demographics: 50% white/50% black or Hispanic, 92% male/8% female. Three patients have reached a study endpoint to date. An HIV isolate has been obtained for each patient at each 3 month visit (100% isolation rate). These isolates are stored in liquid nitrogen. A consensus PBMC-based protocol for determination of HIV drug susceptibility is being finalized with the ACTG and will be applied to all patient HIV isolates.

CONCLUSIONS

Laboratory methods to determine drug susceptibility of patient HIV isolates are being validated. The clinical significance of AZT resistance, measured in vitro, remains uncertain.

REPORT DATE: 09/03/91

WORK UNIT # 8819

DETAIL SUMMARY SHEET

TITLE: Active Immunization of Early HIV Infected Patients with Recombinant
GPl60 HIV Protein: Phase II Study of Toxicity, Immunotherapy, In Vivo
Immunoregulation and Clinical Efficacy

KEYWORDS: gpl60, HIV infection, vaccine therapy

PRINCIPAL INVESTIGATOR: Redfield, Robert LTC MC

ASSOCIATES: Birx, Deborah MAJ MC; Johnson, Steven MAJ MC

SERVICE: HIV Research

STATUS: Ongoing
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the efficacy of recombinant gpl60 (rgpl60) in the treatment of patients with early HIV infection.

TECHNICAL APPROACH

This will be a placebo-controlled, double blind Phase II study consisting of 140 patients in Phase IIA. Patients will be randomized to one of two arms of the study based on their response to a human diploid rabies vaccine. Within each arm of the study, patients will be equally randomized to vaccine or placebo. All volunteers will receive intramuscular injection of 160 ug on days 0, 7, 30, 60, 120, 180, and then at 4 month intervals through completion of the study. Changes in cellular and humoral immune responses, as well as toxicity to rgpl60, will be explored. Based on the results of a 9-month interim analysis, a decision to expand to IIB and add 350 new patients will be made.

PRIOR AND CURRENT PROGRESS

Enrollment for IIA Phase of protocol is completed. No systemic toxicity has been observed, and local reactogenicity, as with the Phase I trial, is minimal.

CONCLUSIONS

Preliminary conclusions pending the execution of interim 9-month analysis to be conducted Spring 1992.

REPORT DATE: 09/03/91

WORK UNIT # 8820

DETAIL SUMMARY SHEET

TITLE: A Phase I Study of the Safety and Immunogenicity of rgp120/HIV-1-111B Vaccine in HIV-1 Seropositive Adult Volunteers

KEYWORDS: gp120, vaccine therapy, HIV infection

PRINCIPAL INVESTIGATOR: Redfield, Robert LTC MC

ASSOCIATES: Birx, Deborah MAJ MC; Johnson, Steven MAJ MC

SERVICE: HIV Research

STATUS: Ongoing

APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the safety and immunogenicity of rgp120 vaccine in asymptomatic HIV-1 infected volunteers, compare the effectiveness of a 3-injection vs. 5-injection schedule, and compare the effect of variable dose levels of rgp120 vaccine.

TECHNICAL APPROACH

This Phase I trial will consist of three groups of 5-10 patients to receive rgp120 in open fashion at increasing doses (100ug to 600ug), on set schedule of 0,1,4,8,16 wks. Two remaining groups will consist of 25 patients each: 20 to receive vaccine, 5 to receive placebo in blinded fashion. All patients receiving vaccine will receive 300ug on differing schedules of 0,1,4,8,16 vs. 0,8,16 wks. Group 1 (open vaccine) will receive an entire schedule (5 shots; 0,1,4,8,16 wks. of 100ug and an identical regimen at 600ug for dose comparison. Alterations in cellular and humoral immune response to HIV specific proteins and changes in vivo and in vitro cellular immune function will be assessed.

PRIOR AND CURRENT PROGRESS

Twenty-four volunteers have been enrolled into the study. The entirety of group 1 has completed the vaccination series at 100ug and have started on 600ug regimen. No systemic reaction to the vaccine has been noted, and local reactogenicity has been mild.

CONCLUSIONS

Preliminarily, vaccination with rgp120 appears to be safe. A complete analysis of immunogenicity will be conducted pending protocol completion.

REPORT DATE: 08/19/91

WORK UNIT # 8400

DETAIL SUMMARY SHEET

TITLE: Relationship Between Marksmanship and Contrast Sensitivity

KEYWORDS: contrast sensitivity, marksmanship

PRINCIPAL INVESTIGATOR: McKee, Morris MAJ MC

ASSOCIATES: Gorski, David MAJ MS

SERVICE: Kenner Army Community Hospital, Fort Lee, VA STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if there is a positive correlation between degree of contrast sensitivity as measured by the VCTS system and performance on the M-16 rifle range.

TECHNICAL APPROACH

A complete optometric examination is performed to rule out disease or other anomalies and visual peculiarities. Then the subject is administered the contrast sensitivity test. The score on the M-16 rifle range is determined. The data are divided into experts and non-qualifiers (or very poor qualifiers). A t-test will be run on the scores to determine if there are any significant differences.

PRIOR AND CURRENT PROGRESS

All actions related to this study ceased with the onset of Desert Shield/Desert Storm. There has been no progress since the last report.

CONCLUSIONS

None as yet.

REPORT DATE: 08/27/91

WORK UNIT # 1501

DETAIL SUMMARY SHEET

TITLE: CALGB 8935 Trimodality Therapy for Stage IIIA Non-small Cell Lung Cancer, Phase II

KEYWORDS: tri-modality, non-small cell, lung cancer

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the feasibility, efficacy, and toxicity of neoadjuvant chemotherapy and postoperative, sequential chemotherapy in the treatment of patients with Stage IIIA non-small cell lung cancer.

TECHNICAL APPROACH

Non-randomized study in which all eligible patients are surgically staged, registered, receive anterior chemotherapy, are evaluated for response, go on to thoracotomy, and on the basis of those findings, receive either posterior chemotherapy and radiotherapy or radiotherapy only.

PRIOR AND CURRENT PROGRESS

A total of three patients have been entered on this study from WRAMC. All three patients had stable disease after anterior chemotherapy but were unresectable at the time of surgery. One patient died of metastatic disease. A total of 50+ patients have been entered nationwide. The study is ongoing.

CONCLUSIONS

No conclusion have been reached.

REPORT DATE: 03/27/91

WORK UNIT # 1502

DETAIL SUMMARY SHEET

TITLE: CALGB 8945 A Phase II Study of Toremifene in Metastatic Breast Cancer

KEYWORDS: breast cancer, metastatic, anti-hormones

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the objective response rate of Toremifene in patients with metastatic breast cancer who are ER and PgR negative. To evaluate duration of response, time to progression, and survival. To assess the toxicities of Toremifene.

TECHNICAL APPROACH

All eligible patients will be assigned the same dose of oral Toremifene, 200 mg twice/day. Treatment will continue until disease progresses or toxicity occurs. Close monitoring for toxicities will be maintained.

PRIOR AND CURRENT PROGRESS

There have not been any patients at WRAMC who have met the eligibility criteria so far.

CONCLUSIONS

The study is ongoing; no conclusions have been reached.

REPORT DATE: 04/05/91

WORK UNIT # 1503

DETAIL SUMMARY SHEET

TITLE: CALGB 8965 Flow Cytometry and Reticulocyte Analysis in Myelodysplastic Syndromes

KEYWORDS: myelodysplasia, flow cytometry

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the relationship of DNA content abnormalities to the subtype and cytogenetics of myelodysplastic syndrome and the conversion to acute leukemia.

TECHNICAL APPROACH

Blood and bone marrow samples are obtained upon study entry and repeated if disease progresses.

PRIOR AND CURRENT PROGRESS

This study opened October 1989. No patients from WRAMC have been entered. Twenty-one patients have been entered nationwide.

CONCLUSIONS

The study is ongoing. No conclusions have been reached.

REPORT DATE: 04/10/91

WORK UNIT # 1504

DETAIL SUMMARY SHEET

TITLE: CALGB 8662 Monitoring Circulating Breast Cancer Associated Antigens
with the 15-3 Radioimmunoassay in Metastatic Breast Cancer

KEYWORDS: metastatic breast cancer, CA15-3 antigens

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the predictive value of a given change in CA15-3 values related to a known clinical event (response, progression or stability).

TECHNICAL APPROACH

10 cc of whole blood is drawn at the time of study entry, at each follow-up visit, and at the time of relapse or disease progression. The plasma is mailed on dry ice to the referenced laboratory.

PRIOR AND CURRENT PROGRESS

This study reopened for patient accrual January 1990. Three patients have been entered since that time; two of those during 1991.

CONCLUSIONS

None so far.

REPORT DATE: 04/05/91

WORK UNIT # 1505

DETAIL SUMMARY SHEET

TITLE: CALGB 8963 Psychological Adaptation of Survivors of Acute Leukemia

KEYWORDS: psychosocial adaptation, survivors, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the long-term psychological impact of a devastating disease, such as acute leukemia, and the impact of surviving treatment.

TECHNICAL APPROACH

The patient has one phone interview and completes one questionnaire from the Department of Psychiatry at Sloan-Kettering Memorial.

PRIOR AND CURRENT PROGRESS

Twelve patients have completed their interview and questionnaire. Fourteen others are eligible and have consented to the study.

CONCLUSIONS

None.

REPORT DATE: 04/05/91

WORK UNIT # 1506

DETAIL SUMMARY SHEET

TITLE: CALGB 8922 Interleukin-2 in Acute Myelogenous Leukemia

KEYWORDS: AML, second remission, interleukin-2

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the activity of interleukin-2 (IL-2) in prolonging remission in acute myelogenous leukemia (AML) patients who are in second remission. To monitor the effect of IL-2 on in vivo activation of NK, LAK and antileukemic cells.

TECHNICAL APPROACH

Patients will be randomized to receive or not receive IL-2. If IL-2 is received, it will be given I.V. by constant infusion 5 days every 2 weeks for 2 months. Blood samples will be drawn before, during, and after treatment. Samples will be drawn twice on patients who do not receive IL-2.

PRIOR AND CURRENT PROGRESS

No patients from WRAMC have been entered into this study.

CONCLUSIONS

Analysis is still in progress.

REPORT DATE: 08/27/91

WORK UNIT # 1508

DETAIL SUMMARY SHEET

TITLE: CALGB 9061 Clinical Significance of Gene Rearrangements in Lymphoma

KEYWORDS: non-Hodgkin's lymphoma, gene rearrangements

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

(1) To utilize the previously collected paraffin blocks of lymph nodes from patients with non-Hodgkin's lymphoma (NHL) treated on CALGB protocols 7951 and 7851 to determine the incidence of Bcl-2-Ig gene translocation; (2) To determine if the presence of this translocation correlates with survival and/or duration of remission; and (3) To examine the peripheral blood of surviving patients for the same.

TECHNICAL APPROACH

Participating institutions will receive a list of eligible patient numbers registered on the above named protocols. Tissue blocks and blood (if possible) will be sent to Dr. Barcos for review. Consent will be obtained from the patient in the event of blood sampling.

PRIOR AND CURRENT PROGRESS

WRAMC had 19 eligible patients for this study. Tissue blocks were mailed to Dr. Barcos on all 19 patients. Blood samples were not obtained, nor consents, as all patients had expired. Review of the quality of these samples is still in progress.

CONCLUSIONS

Specimens still in analysis.

REPORT DATE: 04/10/91

WORK UNIT # 1516-84

DETAIL SUMMARY SHEET

TITLE: CALGB 8364: Immunological Diagnostic Studies in Adult ALL

KEYWORDS: immunology, adult ALL, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: Oct 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of various monoclonal antibodies' cytochemical and conventional lymphoid markers in adult acute lymphatic leukemia (ALL). To correlate the presence of the various markers with the initial and subsequent clinical characteristics of the disease, response rate, and response duration. To determine if marker status changes at relapse.

TECHNICAL APPROACH

Non-randomized study in which all eligible patients being entered on the ALL treatment protocol agree to allow, prior to the initiation of therapy, the submission of six air-dried unstained BM smears for confirmatory cytochemical studies, and 2cc of bone marrow aspirate, along with 7 cc of peripheral blood to a designated CALGB reference laboratory. The same set of samples is again obtained at relapse.

PRIOR AND CURRENT PROGRESS

This study opened in June 1983 as a companion study for ALL patients. It has remained open for accrual as ALL treatment studies have changed. A total of 19 patients have been entered from WRAMC. Five patients are still alive. Four of those patients were entered in 1990. A total of 444 patients have been entered nationwide.

CONCLUSIONS

Study is ongoing. No conclusions have been reached.

REPORT DATE: 08/27/91

WORK UNIT # 1522-84

DETAIL SUMMARY SHEET

TITLE: CALGB 8461: Cytogenic Studies in Acute Leukemia: A Companion to CALGB 8011, 8323, 8321, and 8411

KEYWORDS: cytogenetics, acute leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Sep 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of specific chromosome abnormalities in adult acute non-lymphatic leukemia (ANLL) and acute lymphatic leukemia (ALL).

TECHNICAL APPROACH

All eligible patients are registered to this companion to treatment protocols. A specimen of marrow and blood is obtained at diagnosis and again at relapse.

PRIOR AND CURRENT PROGRESS

This study opened September 1984. A total of 69 patients from WRAMC have been entered. Seven patients have been entered since the last report period. Over 1600 patients have been entered nationwide. The study is ongoing.

CONCLUSIONS

Ongoing analysis. Karyotype reports continue to be reported about every 6 months.

REPORT DATE: 04/05/91

WORK UNIT # 1528-85

DETAIL SUMMARY SHEET

TITLE: CALGB 8541: Adjuvant CAF for Pathologic Stage II Node Positive Breast Cancer: A Comparison of Three Dose Regimens

KEYWORDS: adjuvant therapy, breast cancer, node positive

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Mar 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether there is a dose-dependent relationship between disease-free survival and amount of drug administered for patients with Stage II breast cancer treated with cytoxan, adriamycin, and 5 FU (CAF).

TECHNICAL APPROACH

Randomized study in which all eligible patients receive cytoxan, adriamycin, and 5 FU at one of three different dose levels: Low dose at 300, 30, and 300 mg/m²; standard dose at 400, 40, and 400 mg/m²; or high dose at 600, 60, and 600 mg/m² on day 1 and day 8 for 4 monthly cycles.

PRIOR AND CURRENT PROGRESS

This study opened March 1985; closed April 1991. A total of 49 patients were entered from WRAMC. Five patients have died; five patients came off study due to disease progression. The remaining 39 patients continue to be followed.

CONCLUSIONS

Study is closed -- data being analyzed. Approximately 1,500 patients have been entered nationwide.

REPORT DATE: 05/14/91

WORK UNIT # 1536-85

DETAIL SUMMARY SHEET

TITLE: CALGB 8582: A Comparison of Pentostatin and Alpha Interferon in Splenectomized Patients with Active Hairy Cell Leukemia

KEYWORDS: pentostatin, alpha-interferon, hairy cell leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: May 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare the effectiveness of pentostatin and alpha-interferon in the treatment of hairy cell leukemia. To evaluate the toxicities of the two drugs.

TECHNICAL APPROACH

Patients entered will be randomized to receive either alpha-interferon SQ 3 X week for 13 weeks or pentostatin IV X 2 days, every 2 weeks for 3 months.

PRIOR AND CURRENT PROGRESS

This study opened October 1985. A total of 94 patients have been entered nationwide. Only one patient has been entered from WRAMC. That patient has subsequently died from a non-disease related condition.

CONCLUSIONS

Analysis is still in progress.

REPORT DATE: 08/26/91

WORK UNIT # 1550-86

DETAIL SUMMARY SHEET

TITLE: CALGB 8534: Combination Chemotherapy with Intensive ACE/PCE and Radiation Therapy to the Primary Tumor and Prophylactic Whole Brain Radiation Therapy with or without Warfarin in Limited Small Cell Carcinoma of the Lung

KEYWORDS: lung, carcinoma chemotherapy, radiation

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Aug 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the complete response rate and long-term survival of patients treated with a new combined modality program containing three cycles of ACE followed by concurrent radiation and PCE followed by three cycles of ACE.

TECHNICAL APPROACH

Randomized study in which all eligible patients receive the above listed therapy with or without daily doses of warfarin.

PRIOR AND CURRENT PROGRESS

A total of five patients have been entered on this study. No new patients were entered since the last reporting period. Of the five that were entered, three have died of their disease and two are still being followed for recurrence. Over 300 patients have been entered nationwide. Few patients are seen here that meet the eligibility criteria for Small Cell.

CONCLUSIONS

Ongoing.

REPORT DATE: 08/27/91

WORK UNIT # 1551-86

DETAIL SUMMARY SHEET

TITLE: CALGB 8362: Pharmacokinetics of Ara-C in Patients with Acute
Myelogenous Leukemia, A Companion to CALGB 8525

KEYWORDS: pharmacokinetics, Ara-C, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Sep 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To monitor the plasma levels associated with Ara-C induction therapy and the three dosage levels of Ara-C used in the post-remission therapy in CALGB 8525.

TECHNICAL APPROACH

Non-randomized companion study in which all eligible patients give consent to have four samples of blood drawn during induction therapy and again during the first course of intensification therapy. Blood is then processed and sent to a reference laboratory for drug levels.

PRIOR AND CURRENT PROGRESS

This study originally opened for accrual as a companion to CALGB 8525 in May 1983. It closed after reaching required accrual in October of 1990. The study reopened for accrual as a companion to Relapsed AML protocol 9021 in April of 1991. It is currently still open. No patients have been entered from WRAMC since reopening because no patients have been entered on 9021. A total of 30 patients were entered during the original accrual dates for 8525.

CONCLUSIONS

Anaylsis still in progress.

REPORT DATE: 08/23/91

WORK UNIT # 1554-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8691: Cytosan with or without Interferon for Low Grade Lymphoma

KEYWORDS: cytosan, alpha-interferon, lymphoma

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Dec 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare the effectiveness of cytosan versus cytosan plus alpha-interferon in the management of patients with nodular poorly differentiated lymphocytic and nodular mixed lymphocytic histiocytic lymphoma.

TECHNICAL APPROACH

Randomized study in which all eligible patients receive either cytosan alone or cytosan with alpha-interferon for at least 3 months.

PRIOR AND CURRENT PROGRESS

This study opened December 1986. One patient was entered from WRAMC and received cytosan alone. He relapsed after a complete response. The study closed May 1991. A total of approximately 549 patients were entered nationwide.

CONCLUSIONS

Study is closed. Data being analyzed.

REPORT DATE: 05/14/91

WORK UNIT # 1557-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8791: A Randomized Comparison of Pentostatin Vs. Alpha Interferon in Previously Untreated Patients with Hairy Cell Leukemia

KEYWORDS: deoxycoformycin, alpha-interferon, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Mar 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare deoxycoformycin and alpha interferon with respect to frequency of response, time to response, and duration of relapse free survival among unsplenectomized patients with hairy cell leukemia.

TECHNICAL APPROACH

All eligible patients are registered and stratified to receive either alpha-interferon 3x10⁶ IU SC three times a week for 6 months or to receive deoxycoformycin 4mg/m² IV every 14 days for 6 months.

PRIOR AND CURRENT PROGRESS

Study was suspended in September 1989 and has not reopened. No patients from WRAMC have been entered. A total of 82 patients were entered nationwide.

CONCLUSIONS

Analysis still in progress.

REPORT DATE: 07/29/91

WORK UNIT # 1560-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8642: A Master Protocol to Study Single Agent Chemotherapy Vs. Standard Chemotherapy for Advanced Breast Cancer

KEYWORDS: chemotherapy, cancer, breast

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate single Phase II agents in achieving responses in previously untreated metastatic breast cancer patients.

TECHNICAL APPROACH

Randomized study in which all eligible patients receive either standard CAF therapy or a Phase II agent. Those randomized to receive a Phase II agent are treated for two cycles, then reevaluated for response or progression. If progression occurs, they are switched to CAF therapy. The current Phase II drug under study is Carboplatin.

PRIOR AND CURRENT PROGRESS

A total of nine patients from WRAMC have been entered on this study. Three patients have died of progressive disease, two are alive with progressive disease, and one patient is free of disease two years after treatment on this study. The three patients were entered in 1991 and are still receiving therapy.

CONCLUSIONS

Conclusions have not been finalized.

REPORT DATE: 07/09/91

WORK UNIT # 1564-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8692: Intergroup Study in Metastatic Sarcomas

KEYWORDS: chemotherapy, sarcoma

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if the addition of ifosfamide to doxorubicin and dacarbazine significantly changes the response rate, survival, and toxicity in the therapy of metastatic soft tissue sarcomas.

TECHNICAL APPROACH

Randomized study in which all eligible patients receive either doxorubicin and dacarbazine alone or doxorubicin, dacarbazine, and ifosfamide with mesna. Study is no longer randomized, and only patients with bone sarcomas are now eligible. All eligible patients receive doxorubicin, ifosfamide, dacarbazine, and mesna.

PRIOR AND CURRENT PROGRESS

A total of 11 patients from WRAMC have been entered on this study. Seven patients have died of their disease. The remaining four patients are off the study and are being followed for survival.

CONCLUSIONS

Study is ongoing. No conclusions have been reached.

REPORT DATE: 07/30/91

WORK UNIT # 1567-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8711: Idarubicin in Acute Lymphocytic Leukemia, Relapsed or Failed Induction

KEYWORDS: idarubicin, lymphocytic leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To test the remission induction rate of the idarubicin regimen To identify the toxicity of the idarubicin regimen. To investigate the feasibility of a consolidation regimen containing idarubicin and Ara-C.

TECHNICAL APPROACH

Study has no randomization. All eligible patients receive idarubicin 12.5 mg/m² on days 1, 2, and 3. If remission is documented, idarubicin and Ara-C are given as consolidation therapy. If remission does not occur, reinduction with idarubicin.

PRIOR AND CURRENT PROGRESS

This study closed in October 1990. A total of 44 patients were entered nationwide. Six patients were entered from WRAMC. All six patients have died of their disease.

CONCLUSIONS

Data under analysis.

REPORT DATE: 04/10/91

WORK UNIT # 1568-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8741: A Dose Response Trial of Megace for Advanced Breast Cancer

KEYWORDS: Megace, breast, cancer

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate dose-response relationship for megastrol acetate. To determine relative dose and toxicity to optimize dosing for megastrol acetate. To compare the three dose levels according to the following endpoints: response frequency, time to progression, time to chemotherapy, and time to visceral disease and survival.

TECHNICAL APPROACH

Randomized study in which all eligible patients receive one of three dose levels of Megace: 160 mg, 800 mg, or 1600 mg per day.

PRIOR AND CURRENT PROGRESS

This study opened July 1987. A total of eight patients have been entered from WRAMC. No patients were entered during 1990. Three of those eight patients have died, three have had disease progression, and two are still in follow-up. The study closed March 1991.

CONCLUSIONS

No conclusions have been reached.

REPORT DATE: 04/05/91

WORK UNIT # 1573-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8762: Molecular Subtypes in Acute Lymphatic Leukemia with Philadelphia Chromosome

KEYWORDS: Philadelphia chromosome, ALL

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of pH positivity in patients with previously untreated acute lymphatic leukemia (ALL).

TECHNICAL APPROACH

Non-randomized comparison study in which all eligible patients who consent to allow a sample of blood and bone marrow to be sent to a reference laboratory at the time of diagnosis, first intensification, and at relapse.

PRIOR AND CURRENT PROGRESS

This study opened October 1987. A total of five patients have been entered from WRAMC. Four of these patients were entered in 1990. A total of three continue to be followed in their remission. A total of 97 patients have been entered nationwide.

CONCLUSIONS

No conclusions have been reached. This is an ongoing study. The initial goal of the study was to accrue approximately 250 patients over a 5 year period.

REPORT DATE: 04/05/91

WORK UNIT # 1574-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8763: Immunoglobulin and T Cell Receptor Gene Rearrangement in Adult Acute Lymphatic Leukemia

KEYWORDS: immunoglobulin, T-cell receptor, ALL

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of Ig and T-cell receptor gene rearrangements from samples of patients with previously untreated adult ALL.

TECHNICAL APPROACH

Non-randomized companion study in which all eligible patients who consent to allow a sample of bone marrow and blood to be sent to CALGB reference laboratory at the time of diagnosis, prior to first intensification, and at relapse.

PRIOR AND CURRENT PROGRESS

This study opened October 1987. Five patients have been entered from WRAMC. Four of those patients were entered in 1990. Two patients continue to be followed in remission.

CONCLUSIONS

The study is ongoing. No conclusions have been reached.

REPORT DATE: 09/24/91

WORK UNIT # 1575-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8765: Analysis of Proto-Oncogene Expression in Acute Myelogenous Leukemia

KEYWORDS: proto-oncogene, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence and clinical significance of proto-oncogene expression in ANLL blasts.

TECHNICAL APPROACH

Prior to initiation of therapy and at relapse, 2 cc's of marrow and 10 cc's of blood are sent to a CALGB reference laboratory for analysis.

PRIOR AND CURRENT PROGRESS

A total of 22 patients have been entered on this study with appropriate blood and BM samples sent to the CALGB reference laboratory. Of those 22 patients, 11 remain to be followed (7 have died, 2 did not attain a complete remission, and 2 have relapsed with samples sent). The study was closed to accrual August 1991.

CONCLUSIONS

Analysis of data is ongoing. No conclusions have been reached.

REPORT DATE: 04/10/91

WORK UNIT # 1576-87

DETAIL SUMMARY SHEET

TITLE: CALGB 8766: Immunologic and Molecular Diagnostic Studies in Chronic Lymphatic Leukemia

KEYWORDS: immunology, lymphocytic leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of the expression of the antigens in peripheral blood samples of consecutive patients with previously untreated chronic lymphatic leukemia (CLL).

TECHNICAL APPROACH

Non-randomized study in which all eligible patients are registered only. At study entry, 10-20 ml of blood is collected and mailed by courier to a CALGB reference laboratory for analysis.

PRIOR AND CURRENT PROGRESS

This study opened in December 1987. A total of 17 patients have been entered; one patient has died. Three of those patients were entered in 1989; none in 1990. Accrual to this study was suspended in May 1990. No further samples are required. The remaining 16 patients are being followed for survival.

CONCLUSIONS

A total of 205 patients were entered nationwide. The data is still being analyzed.

REPORT DATE: 03/22/91

WORK UNIT # 1577-80

DETAIL SUMMARY SHEET

TITLE: CALGB 8361: Immunologic Diagnostic Studies in AML (blood drawing phase); previously CALGB 7921) CALGB 8321: A Comparative Study of 3 Remission Induction Regimens and 2 Maintenance Regimens for AML (treatment phase); previously CALGB 7921

KEYWORDS: immunology, oncology, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Dec 1981

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine the incidence of various markers in acute myelogenous leukemia (AML); b) To correlate the presence of these markers and the surface antigen phenotype they determine with the FAB histological classification; and c) To correlate the presence of the various markers with the initial and subsequent clinical characteristics of the disease.

TECHNICAL APPROACH

All eligible patients are registered prior to the initial therapy. From the diagnostic bone marrow procedure, 2 cc of bone marrow and 7 cc of peripheral blood are collected and sent by express mail to the CALGB reference laboratory for analysis and confirmation of classification. Samples are again obtained at relapse.

PRIOR AND CURRENT PROGRESS

This study remains open. A total of 56 patients have been entered since the first approval date; of that total, one patient was entered in 1990 and two patients thus far have been entered in 1991.

CONCLUSIONS

This study is ongoing. No conclusions have been reached.

REPORT DATE: 11/13/90

WORK UNIT # 1579-88

DETAIL SUMMARY SHEET

TITLE: CALGB 8861: Monitoring Circulating Breast Cancer-Associated 15-3
Antigen in Stage II Breast Cancer

KEYWORDS: antigen, breast cancer, Stage II

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Jan 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the predictive value of rising CA15-3 levels in patients who are clinically free of recurring disease.

TECHNICAL APPROACH

Ten cc's of whole blood is collected prior to first therapy, at 28 day intervals during therapy, at 4 month intervals for 2 years, and then every 6 months for 4 years. Blood is processed at WRAMC and shipped to CALGB approved reference laboratory for analysis.

PRIOR AND CURRENT PROGRESS

This study opened December 1988. A total of 12 patients have been entered at WRAMC; 4 of those during 1990. One patient was taken off study for progressive disease; the remaining 11 patients continue to be followed and blood samples are being collected.

CONCLUSIONS

Analysis is still in progress.

REPORT DATE: 12/03/90

WORK UNIT # 1581-80

DETAIL SUMMARY SHEET

TITLE: CALGB 8363: Clonal Excess Determination in Non-Hodgkin's Lymphoma
(Blood drawing phase); previously CALGB 7851/7951 (Treatment phase)

KEYWORDS: clonal excess, lymphoma, non-Hodgkin's

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Apr 1980

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To monitor clonal excess in peripheral blood of patients with B cell lymphomas on defined protocols in a prospective, sequential fashion.

TECHNICAL APPROACH

Non-randomized companion protocol to existing CALGB lymphoma treatment protocols. Eligible patients submit 50cc of peripheral blood prior to being initially treated, again at the time of their CR, and then every 4 months until relapse or at relapse.

PRIOR AND CURRENT PROGRESS

This study has been open to patient accrual since April 1980. A total of 16 patients have been entered; 6 have expired, and 3 have relapsed and are off study. Blood specimens continue to be collected on the 7 remaining patients. No further patients have been added since suspension of the protocol in May 1990.

CONCLUSIONS

None so far. Protocol suspended pending analysis of data.

REPORT DATE: 07/30/91

WORK UNIT # 1583-88

DETAIL SUMMARY SHEET

TITLE: CALGB 8862: A Pharmacodynamic Study of Amonafide

KEYWORDS: amonafide, pharmacodynamics

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine feasibility of conducting a multi-institutional pharmacodynamic study employing limited sampling points. To examine the relationships between pharmacokinetic characteristics of amonafide and clinical outcome. This study is a companion to treatment protocol CALGB 8642.

TECHNICAL APPROACH

All eligible patients give consent for the collection of blood samples (30cc each, prior to treatment, 45 minutes and 24 hours after treatment) for one course of therapy only. Blood is then processed and sent to a CALGB reference laboratory for analysis.

PRIOR AND CURRENT PROGRESS

No patients have been entered on this study. The four patients we have entered on the treatment protocol, since the last report date, were not randomized to the amonafide arm. A total of 62 patients have been entered nationwide.

CONCLUSIONS

No conclusions have been reached.

REPORT DATE: 08/27/91

WORK UNIT # 1584-88

DETAIL SUMMARY SHEET

TITLE: CALGB 8896: An Intergroup Study of Adjuvant Therapy of Primary Colon Cancer

KEYWORDS: chemotherapy, adjuvant, colon Ca

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare relative toxicity and efficacy of three approaches (low dose leukovorin + 5FU, high dose leukovorin + 5FU, observation) to treatment of patients with Duke's B or C colon cancer post-curative surgery.

TECHNICAL APPROACH

Randomized study in which all eligible patients are stratified according to extent, obstruction, and metastasis to receive surgery alone or surgery followed by low dose chemotherapy or high dose chemotherapy.

PRIOR AND CURRENT PROGRESS

A total of 10 patients from WRAMC have been entered on this study; 3 since the last report period. All patients continue to be followed here, without evidence of recurrence. Over 475 patients have been entered nationwide. Study is ongoing.

CONCLUSIONS

Too early for conclusions.

REPORT DATE: 07/29/91

WORK UNIT # 1586-88

DETAIL SUMMARY SHEET

TITLE: CALGB 8811: A Phase II Study of an Intensive Chemotherapy Regimen for Acute Lymphocytic Leukemia

KEYWORDS: chemotherapy, lymphocytic, leukemia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine feasibility and toxicity of intensive chemotherapy for untreated adults with ALL. To determine response rate and disease free survival of proposed five drug induction regimen.

TECHNICAL APPROACH

Non-randomized study in which all eligible patients receive an induction regimen containing Cytosan, doxorubicin, prednisone, vincristine and L-asparaginase. If remission occurs, four more courses of intensification are given, including radiation therapy.

PRIOR AND CURRENT PROGRESS

This study opened November 1988. A total of seven patients from WRAMC were entered. Two of those patients have died, two moved away and went off treatment (still alive), and three are still in complete remission. A total of 148 patients have been entered nationwide. The study closed June 1991.

CONCLUSIONS

The data is still be analyzed.

REPORT DATE: 04/10/91

WORK UNIT # 1587-88

DETAIL SUMMARY SHEET

TITLE: CALGB 8864: Assessing Quality of Life During a Dose Response Trial of Megace for Advanced Breast Cancer Patients

KEYWORDS: Megace, breast cancer, quality of life

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare differences in quality of life of three groups of advanced breast cancer patients receiving different dose levels of megestrol acetate over a 3 month period.

TECHNICAL APPROACH

All patients who are entered on CALGB 8741 are asked to participate in an interview process. The written and phone report occurs three different times; i.e., day 1 of therapy, month 1 of therapy, and month 3 of therapy.

PRIOR AND CURRENT PROGRESS

This study opened November 1988 and closed March 1991. A total of three patients were entered from WRAMC. Total accrual nationwide was around 121 patients.

CONCLUSIONS

The data is still being analyzed.

REPORT DATE: 08/30/90

WORK UNIT # 1588-88

DETAIL SUMMARY SHEET

TITLE: CALGB 8894: A Phase III Intergroup Study of Adjuvant Therapy of
Primary Rectal Cancer

KEYWORDS: adjuvant therapy, rectal cancer

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare local recurrence rates; rates of distant metastasis, disease free survival, and overall survival in patients having resection of rectal carcinoma treated with sequential chemotherapy and radiotherapy.

TECHNICAL APPROACH

Randomized study in which all eligible patients are assigned a treatment of either 5FU and methyl CCNU plus radiation with bolus 5FU or CI 5FU, or 5FU alone plus radiation with bolus 5FU or CI 5FU.

PRIOR AND CURRENT PROGRESS

This study opened in November 1988 and closed in August 1990. Two patients have been entered on this study. To date, both patients have completed therapy and are in follow-up phase. Both are without evidence of disease.

CONCLUSIONS

None. Data still being reviewed.

REPORT DATE: 04/10/91

WORK UNIT # 1589-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8865: Pharmacokinetics of Megace in Patients with Advanced Breast Cancer

KEYWORDS: breast cancer, hormone therapy, serum Megace levels

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare the relationship between the level of Megace in the bloodstream and the effect of Megace on the cancer. To evaluate the usefulness of this comparison in the treatment of advanced breast cancer.

TECHNICAL APPROACH

A 7 ml blood sample is drawn prior to therapy and again before each morning dose on day 1, 4, 6, 8, 10, 12, and 14. The patient is admitted to the hospital for a 24 hour period at some point between day 14 and 18. During this time, 11 venous blood samples are drawn at specified intervals.

PRIOR AND CURRENT PROGRESS

No patients from WRAMC were entered on this study. Eleven patients were entered nationwide. The study closed March 1991.

CONCLUSIONS

None, so far.

REPORT DATE: 02/07/91

WORK UNIT # 1592-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8793 A Clinical Trial to Evaluate the Natural History and Treatment of Patients with Noninvasive Adenocarcinoma and the Lobular Carcinoma in Situ Registry

KEYWORDS: natural history, adenocarcinoma, lobular carcinoma

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the efficacy of postoperative breast irradiation following segmental mastectomy +/- ancillary dissection in patients with noninvasive intraductal adenocarcinoma.

TECHNICAL APPROACH

All eligible patients are randomized to either observation only or breast irradiation.

PRIOR AND CURRENT PROGRESS

The study was open to accrual in February 1989. No patients were entered on study. The protocol was officially closed to accrual by CALGB in December 1990.

CONCLUSIONS

None. Analysis is in progress.

REPORT DATE: 05/14/91

WORK UNIT # 1595-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8961 RAS Mutations in Myelodysplasia

KEYWORDS: RAS, oncogenes, myelodysplasia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the prevalence of mutant RAS genes in myelodysplasia. To determine if the presence of such a mutation predicts subsequent leukemic development.

TECHNICAL APPROACH

Non-randomized, non-treatment protocol in which all eligible patients are registered. Blood and bone marrow samples and slides are obtained at entry and again when acute leukemia develops.

PRIOR AND CURRENT PROGRESS

This study opened at WRAMC in April 1989. A total of four patients have been entered; one patient in 1990. All four patients have died. A total of 75 patients have been entered nationwide.

CONCLUSIONS

Analysis is still in progress.

REPORT DATE: 08/26/91

WORK UNIT # 1596-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8897 Evaluation of Adjuvant Therapy for Node Negative Primary Breast Cancer, Phase III

KEYWORDS: adjuvant, node negative, breast cancer

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare disease free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard CMF or CAF chemotherapy. To assess value of the addition of tamoxifen in these patients.

TECHNICAL APPROACH

This is a complicated study in which eligible patients are registered as low, uncertain, or high risk patients. Low risk patients are followed with no therapy. Uncertain risk patients undergo flow cytometry to be categorized as low or high. Those categorized as high risk patients, plus all other known high risks, are then randomized to CMF, CMF with tamoxifen, CAF, or CAF with tamoxifen.

PRIOR AND CURRENT PROGRESS

Seventeen additional patients have been entered in this study since the last report period. The total number of patients registered from WRAMC is 24. Nine patients were in the high risk arm, five patients were in the uncertain risk arm, and 10 patients were in the low risk arm. All patients under low and uncertain risk had tissue blocks sent for DNA analysis. Analysis of the tissue blocks on the uncertain risk patients resulted in two low risk and three high risk. Two patients registered as high risk have had recurrences. One high risk patient withdrew consent for further therapy. All other patients continue to be followed.

CONCLUSIONS

Data is still being collected.

REPORT DATE: 10/17/90

WORK UNIT # 1597-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8921 A Phase II Study of 5-Azacytidine in Myelodysplastic Syndromes

KEYWORDS: 5-azacytidine, myelodysplasia

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Cancer & Leukemia Group B

APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine those myelodysplastic syndromes that will respond optimally to subcutaneous azacytidine. To evaluate azacytidine toxicity.

TECHNICAL APPROACH

Non-randomized study in which all eligible patients are registered and receive 5-azacytidine 75mg/m²/d x 7, are assessed by bone marrows, and receive more drug on day 29, etc.

PRIOR AND CURRENT PROGRESS

CALGB closed this study in October 1990. No patients at WRAMC were entered during the year the study was open because no eligible patients were found.

CONCLUSIONS

None.

REPORT DATE: 07/30/91

WORK UNIT # 1598-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8952 Combination Chemotherapy for Advanced Hodgkin's Disease,
Phase III

KEYWORDS: chemotherapy, Hodgkin's disease

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare ABVD to the MOPP/ABV hybrid as therapy for patients with Hodgkin's disease in terms of complete response rates, disease free survival, failure free survival, and both intermediate and long-term toxicities.

TECHNICAL APPROACH

Randomized study in which eligible patients receive either ABVD or the MOPP/ABV hybrid combination for a minimum of six cycles unless progression is documented.

PRIOR AND CURRENT PROGRESS

Two patients have been entered in this study since activation in February 1990. Both patients have had a response and now have stable disease. A total of 163 patients have been entered nationwide.

CONCLUSIONS

Ongoing; no conclusions have been reached.

REPORT DATE: 08/23/91

WORK UNIT # 1599-89

DETAIL SUMMARY SHEET

TITLE: CALGB 8964 Pathology Review of Long Term Survivors in Small Cell Lung Cancer: A Case Control Study

KEYWORDS: pathology, long-term survivors, small cell lung cancer

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine
SERVICE: Cancer & Leukemia Group B

STATUS: Completed
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare differences in histology on biopsy or cytology material, according to the WHO classification, on patients who are long-term survivors and controls in a blended design.

TECHNICAL APPROACH

Long-term survivors of previous small cell lung cancer protocols are identified, pathology materials are retrieved and sent to CALGB pathology office, and blocks are then coded, cut, and returned. Pathology review is carried out, with that data then coded and sent to central office.

PRIOR AND CURRENT PROGRESS

Pathology material was submitted for review on 28 patients. This completes our submission requirement. The study is now closed.

CONCLUSIONS

Analysis is in progress.

REPORT DATE: 05/08/91

WORK UNIT # 1243

DETAIL SUMMARY SHEET

TITLE: Percutaneous Balloon Valvuloplasty for Patients with Mitral Stenosis or Aortic Stenosis: A Pilot Study

KEYWORDS: valvuloplasty, aortic stenosis, mitral stenosis

PRINCIPAL INVESTIGATOR: Moore, John LTC MC

ASSOCIATES: Ross, Terence, MAJ MC; Banks, Alan MAJ MC

DEPARTMENT: Department of Medicine

SERVICE: Cardiology Service

STATUS: Ongoing

APPROVAL DATE: Oct 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of percutaneous balloon valvuloplasty (PBV) in adults with aortic or mitral stenosis.

TECHNICAL APPROACH

Symptomatic patients with mitral stenosis and aortic stenosis will be offered PBV as an option to standard surgical valve replacement. PBV will be performed, with immediate and short-term (6 months) hemodynamic, aortographic, and echocardiographic evaluation.

PRIOR AND CURRENT PROGRESS

To date, 38 patients have been enrolled in the study and have undergone balloon aortic valvuloplasty, and 35 patients have undergone balloon mitral valvuloplasty. In the past year, six patients have undergone balloon aortic valvuloplasty and three patients have undergone balloon mitral valvuloplasty. The only significant complication which occurred in the past year was a femoral artery pseudo-aneurysm which was repaired without complication. The great majority of patients have had significant clinical improvement following the procedure, and the overall complication rate is within accepted norms.

CONCLUSIONS

Much has been learned about the short- and long-term success of balloon valvuloplasty. In particular, the study has pointed out the limited success of aortic valvuloplasty as a definitive treatment for calcific aortic stenosis. It has also delineated the importance of proper patient selection for mitral valvuloplasty.

REPORT DATE: 07/15/91

WORK UNIT # 1245

DETAIL SUMMARY SHEET

TITLE: A Double Blind Study of the Safety and Efficacy of Multiple Intravenous Infusions of Disodium EDTA in Patients with Obstructive Peripheral Arterial Disease and Intermittent Claudication

KEYWORDS: EDTA, claudication

PRINCIPAL INVESTIGATOR: Wortham, Dale COL MC

ASSOCIATES: Bigham, Peter CPT MC

DEPARTMENT: Department of Medicine

SERVICE: Cardiology Service

STATUS: Ongoing

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the intravenous administration of EDTA in subjects with peripheral vascular disease manifested by intermittent claudication.

TECHNICAL APPROACH

Thirty weekly intravenous administrations at two different dosage levels will be given. The effect on the symptom of exercise tolerance will be compared, and the drug response will be evaluated by measuring the distances walked during treadmill examination.

PRIOR AND CURRENT PROGRESS

There are currently three active patients. A total of 23 patients have been enrolled at WRAMC. Recruitment has been slow, and the percentage of patients who qualify is low due to the strict entry criteria.

CONCLUSIONS

The study is progressing slowly without adverse events.

REPORT DATE: 05/09/91

WORK UNIT # 1249

DETAIL SUMMARY SHEET

TITLE: Multicenter Study of Silent Ischemia

KEYWORDS: silent ischemia, myocardial infarction, unstable angina

PRINCIPAL INVESTIGATOR: Rogan, Kevin MAJ MC

ASSOCIATES: Gorman, Patrick CPT MC

DEPARTMENT: Department of Medicine

SERVICE: Cardiology Service

STATUS: Ongoing

APPROVAL DATE: Dec 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Heart patients can have brief episodes of silent myocardial ischemia (MI) which are reflected on the electrocardiogram without accompanying symptoms. The meaning of ischemia without symptoms is uncertain. The purpose of this study is to find out whether silent ischemia is a predictor of future complications, such as myocardial infarction, development of unstable angina, or sudden death.

TECHNICAL APPROACH

One to six months after hospitalization for acute MI, unstable angina or congestive heart failure with ischemic etiology, study subjects will have a physical exam, cardiovascular history taken, a 24-hour Holter recording, routine ECG, a thallium exercise test and a psychological profile questionnaire. Follow-up visits include a brief interview to assess health status and, on some occasions, an ECG. The 24 hour Holter is repeated once (at the first follow-up visit).

PRIOR AND CURRENT PROGRESS

This study currently has 38 patients enrolled. Thirty-seven are active, with one in inactive status secondary to demographic location. Enrollment was completed 30 Nov 90. Patients are currently receiving follow-up visits every 4-6 months as protocol dictates. Patients will be followed until 30 Nov 91. In December 1991, a final patient visit will be conducted for study completion.

CONCLUSIONS

Active enrollment completed as of 30 Nov 90. Follow-up continuing through November 1991. Study to be completed in December 1991.

REPORT DATE: 08/07/91

WORK UNIT # 1253

DETAIL SUMMARY SHEET

TITLE: Diastolic Dysfunction of the Left Ventricle as a Predictor of
Doxorubicin Cardiotoxicity: A Pilot Study

KEYWORDS: diastolic dysfunction, cardiotoxicity, Adriamycin

PRINCIPAL INVESTIGATOR: Rogan, Kevin MAJ MC
ASSOCIATES: Dykstra, Gary MAJ MC; Norby, Eric MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Cardiology Service

STATUS: Completed
APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the ability of noninvasive techniques, such as Doppler and MUGA testing of diastolic function, to assess early complications of Adriamycin therapy on cardiac function. Are these tests as good as endomyocardial biopsy? Are they good at early discrimination of cardiac toxicity?

TECHNICAL APPROACH

Comparison of standard Doppler parameters of diastolic function (peak filling rates, early/late diastolic filling ratios) and MUGA parameters of diastolic function (time to peak filling, peak filling rate) with endomyocardial biopsy and invasive hemodynamic monitoring in patients who are to receive Adriamycin. Serial assessment by noninvasive means is done at time zero and after 150 mg/M2 and after 300 mg/M2 of Adriamycin. Biopsy is performed at 300 mg/M2.

PRIOR AND CURRENT PROGRESS

This study is being terminated at this time due to departure of the principal investigator and associate investigators. No patients were enrolled during this past fiscal year.

CONCLUSIONS

None.

REPORT DATE: 10/09/91

WORK UNIT # 1254

DETAIL SUMMARY SHEET

TITLE: Cardiac Arrhythmia Suppression Trial (CAST)

KEYWORDS: encainide, flecainide, myocardial infarction

PRINCIPAL INVESTIGATOR: Weston, Lawrence MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Cardiology Service

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To test whether suppression of asymptomatic ventricular arrhythmias after myocardial infarction would reduce mortality from arrhythmic death.

TECHNICAL APPROACH

Patients between 6 days and 2 years following myocardial infarction, with greater than 6VPD's/hr on Holter monitor, and reduced left ventricular ejection fractions, will be enrolled in open label titration therapy with encainide, flecainide or moricizine. After demonstrating arrhythmia suppression, patients will then be placed in the double-blinded, placebo controlled period and followed. Because of the publication of interim results from this study in April 1989 and the necessary removal of encainide and flecainide from the study, the protocol was changed in September 1989, with the study continuing with moricizine only.

PRIOR AND CURRENT PROGRESS

In August 1991 the National Heart, Lung and Blood Institutes discontinued the study because of the remote likelihood of benefit to continued therapy. The three patients on blinded moricizine therapy were contacted and have discontinued therapy. No adverse outcomes have been observed in these patients.

CONCLUSIONS

The results of CAST/CAST II demonstrate that the treatment of asymptomatic ventricular ectopy with encainide, flecainide or moricizine in post-myocardial patients is associated with a higher mortality compared to the placebo.

REPORT DATE: 06/26/91

WORK UNIT # 1256

DETAIL SUMMARY SHEET

TITLE: High Resolution Ambulatory Holter Monitoring in Preoperative Cardiac
Evaluation of Vascular Surgery Patients

KEYWORDS: Holter, preoperative evaluation, vascular surgery

PRINCIPAL INVESTIGATOR: Cambier, Patrick CPT MC

DEPARTMENT: Department of Medicine
SERVICE: Cardiology Service

STATUS: Ongoing
APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To demonstrate diagnostic utility in high resolution Holter monitoring preoperatively to assess vascular surgical risk of myocardial ischemia.

TECHNICAL APPROACH

Preoperative vascular patients who frequently cannot exercise (to allow traditional stress testing) need alternative means of assessing preoperative cardiovascular risk. High resolution Holter monitoring may provide such insight.

PRIOR AND CURRENT PROGRESS

The total enrollment is almost 50. The study is to completed within 1 year.

CONCLUSIONS

No objective data was obtained by Holter monitoring. Several clinical endpoints were reached in the clinical phase of the study.

REPORT DATE: 06/07/91

WORK UNIT # 1257

DETAIL SUMMARY SHEET

TITLE: Implantation by Catheter of Prostheses to Close Arterial Septal Defects
in Two Adolescent Patients at WRAMC

KEYWORDS: arterial septal defects, ASD

PRINCIPAL INVESTIGATOR: Moore, John LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Cardiology Service

STATUS: Completed
APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Protocol involves implanting two arterial septal defect (ASD) closure devices into two patients with ASD's.

TECHNICAL APPROACH

Transcatheter/percutaneous technique, as described in protocol.

PRIOR AND CURRENT PROGRESS

Two patients had successful implantation of the devices without complications. At 6 month's follow-up, one patient had complete ASD closure and no problems. The second patient had a residual ASD with bidirectional shunting. She elected to have the device removed surgically and the ASD closed. This has been accomplished without complications.

CONCLUSIONS

The ASD device looks promising. The patients are part of a multi-institutional collaborative study, so conclusions regarding this experience are limited.

REPORT DATE: 07/18/91

WORK UNIT # 1258

DETAIL SUMMARY SHEET

TITLE: Combined Effects of Angiotensin-Converting Enzyme Inhibitors and Digoxin in the Chronic Treatment of Idiopathic Dilated Cardiomyopathy

KEYWORDS: dilated cardiomyopathy, ACE-inhibitor, digoxin

PRINCIPAL INVESTIGATOR: Hull, Robert CPT MC

ASSOCIATES: Rogan, Kevin MAJ MC; Wortham, Dale COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Cardiology Service

APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the clinical efficacy of long-term oral digoxin therapy in normal sinus rhythm in patients with underlying idiopathic dilated cardiomyopathy already maintained on chronic ACE-inhibitor therapy. Long-term benefit is to be assessed in terms of overall drug requirements, functional class, quality of life assessment, exercise capacity, and left ventricular ejection fraction.

TECHNICAL APPROACH

Patients will be maintained on oral ACE-inhibitors and undergo baseline assessment as described above. They then will undergo 4-month study periods involving crossover with digoxin/placebo. Study periods will be doubled-blinded, and there will be a 1-month washout period between phases. Each patient will undergo a clinic assessment at the 2-month mark into each period, and at 4 months, each patient will have all baseline assessments repeated.

PRIOR AND CURRENT PROGRESS

Ten patients have been enrolled to date. Five patients have completed the protocol in its entirety. Three patients experienced recurrent congestive heart failure (meeting a study endpoint) in the digoxin withdrawal phase, thus terminating their study participation. One patient with an ejection fraction of 26% experienced sudden cardiac death while receiving digoxin in the blinded phase of the protocol. This is not unexpected since sudden cardiac death accounts for a significant number of deaths in patients with severe left ventricular dysfunction, and these patients are routinely receiving digoxin. Two patients are currently enrolled but have not yet completed the protocol.

CONCLUSIONS

This study is ongoing with enrollment at half of the projected study participation.

REPORT DATE: 11/27/91

WORK UNIT # 1259

DETAIL SUMMARY SHEET

TITLE: Two Dimensional Ultrasound Imaging of Peripheral and Coronary Arteries

KEYWORDS: intravascular image, coronary, peripheral

PRINCIPAL INVESTIGATOR: Woods, Roderick MAJ MC

ASSOCIATES: Vernalis, Marina LTC MC; Wortham, Dale COL MC

DEPARTMENT: Department of Medicine

STATUS: Terminated

SERVICE: Cardiology Service

APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Qualitative and quantitative comparison of angiographic vs. intravascular arterial images to determine the advantages and limitations of each imaging technology in the assessment of arterial pathology.

TECHNICAL APPROACH

Diagnostic arteriograms from routine peripheral and coronary studies are compared with intravascular ultrasound images of the same sites. An 8-French peripheral and 5-French coronary catheter will be used for ultrasonic imaging via femoral artery access. Coronary ultrasonic images will only be obtained from subjects undergoing percutaneous transluminal coronary angioplasty.

PRIOR AND CURRENT PROGRESS

This protocol has been administratively terminated.

CONCLUSIONS

This protocol has been administratively terminated.

REPORT DATE: 05/21/91

WORK UNIT # 1260

DETAIL SUMMARY SHEET

TITLE: Antiarrhythmic Therapy in Congestive Heart Failure, VA Cooperative Study #320

KEYWORDS: heart failure, antiarrhythmic therapy, survival

PRINCIPAL INVESTIGATOR: Weston, Lawrence MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Cardiology Service

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether the treatment of ventricular arrhythmias with amiodarone prolongs survival by reducing sudden death in patients with congestive heart failure.

TECHNICAL APPROACH

The study is a multi-center, randomized, double-blinded, placebo-controlled trial of the effects of amiodarone on survival in patients with congestive heart failure. Patients qualifying for enrollment must have significant heart failure and ventricular ectopy on ambulatory ECG monitoring. Patients are then randomized to either amiodarone or placebo and then followed for the end points of the study. No modifications have been made to the original protocol methods.

PRIOR AND CURRENT PROGRESS

To date, nine patients from Walter Reed have been enrolled in the protocol. Enrollment in the study was temporarily stopped when the study nurse was called to active duty for Desert Shield/Desert Storm. Two patients have withdrawn from the study alive; one because of the frequency of follow-up visits (every month) and the distance he was required to travel; and one because he moved to Louisiana. The remaining seven patients continue to be followed. No unexpected or serious adverse reactions have been encountered, and no patient has had to discontinue taking the study drug because of adverse reactions. No clear benefit has been demonstrated in any patient.

CONCLUSIONS

The study is continuing with over 300 patients enrolled study-wide. The results are expected to provide important information regarding the management of these high-risk patients.

REPORT DATE: 03/08/91

WORK UNIT # 1261

DETAIL SUMMARY SHEET

TITLE: Use of a New Valvuloplasty Catheter for Percutaneous Balloon Dilation
of Stenotic Pulmonary Valves

KEYWORDS: valvuloplasty, catheter, pulmonic stenosis

PRINCIPAL INVESTIGATOR: Moore, John LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Cardiology Service

STATUS: Completed
APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine efficacy of a new valvuloplasty catheter.

TECHNICAL APPROACH

Catheter will be used in selected patients with pulmonic stenosis to perform percutaneous valvuloplasty.

PRIOR AND CURRENT PROGRESS

This study was terminated before any patients were enrolled. The company sponsoring the project decided not to develop the valvuloplasty catheter.

CONCLUSIONS

None.

REPORT DATE: 04/01/91

WORK UNIT # 1262

DETAIL SUMMARY SHEET

TITLE: Utility of Transesophageal Echocardiography in Evaluation of Young Patients with Unexplained Cerebral Ischemia and Infarction

KEYWORDS: stroke, echocardiography, embolism

PRINCIPAL INVESTIGATOR: Gaither, Neal MAJ MC

ASSOCIATES: May, Eugene CPT MC

DEPARTMENT: Department of Medicine

SERVICE: Cardiology Service

STATUS: Ongoing

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the role of echocardiography for detecting the source of embolic stroke in young patients. To compare the diagnostic yield of transthoracic versus transesophageal echocardiography for detection of "source of embolism" in young patients.

TECHNICAL APPROACH

Transthoracic and transesophageal echocardiography with saline contrast and Valsalva's maneuver. Further evaluation if clinically appropriate.

PRIOR AND CURRENT PROGRESS

To date, 23 patients have been enrolled. Twelve controls have been recruited, with data kept on file. Initial echocardiographic interpretation and appropriate clinical management have been undertaken. Blinded interpretation of the echocardiograms has not been performed.

CONCLUSIONS

Study remains in progress, with nearly half of the anticipated number of patients enrolled thus far. We predict an additional 18 months of recruitment will result in completion of the objectives of the study.

REPORT DATE: 06/12/91

WORK UNIT # 1263

DETAIL SUMMARY SHEET

TITLE: Toxicology of Vasoactive-Heme Reactive Drugs

KEYWORDS: endothelial derived, relaxing factor, nitrosylated hemoglobin

PRINCIPAL INVESTIGATOR: Cantilena, Louis MD PhD

ASSOCIATES: Frasure, Susan MD

DEPARTMENT: Department of Medicine

SERVICE: Cardiology Service

STATUS: Completed

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if nitrosylated hemoglobin (NO-Hb) is present in patients receiving vasodilator drugs.

TECHNICAL APPROACH

Blood specimens were obtained from patients receiving nitrosylated intravenously. RBC's were separated and Hb analyzed by ESR for the presence of NO-Hb.

PRIOR AND CURRENT PROGRESS

Several of the 25 patients enrolled in the study were found to have NO-Hb in association with their receiving intravenous nitroglycerin.

CONCLUSIONS

The vasoactive drug, nitroglycerin, likely produces NO-Hb in patients.

REPORT DATE: 06/12/91

WORK UNIT # 1805

DETAIL SUMMARY SHEET

TITLE: Use of Isotretinoin in Prevention of Basal Cell Carcinoma

KEYWORDS: basal cell, prevention, isotretinoin

PRINCIPAL INVESTIGATOR: Benson, Paul MAJ MC

ASSOCIATES: Sperling, Leonard MAJ MC

DEPARTMENT: Department of Medicine

SERVICE: Dermatology Service

STATUS: Ongoing

APPROVAL DATE: May 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 217,394 Total: \$ 217,394

STUDY OBJECTIVE

a) To evaluate the effectiveness of low dosage levels of isotretinoin in reducing the incidence of basal cell carcinomas in a high risk population; b) To examine possible side effects associated with long-term administration of low doses of isotretinoin.

TECHNICAL APPROACH

The study is a double-blind randomized clinical trial to evaluate the efficacy of isotretinoin in reducing the incidence of basal cell carcinoma. A minor modification to the original protocol made during the previous year is that two consecutive fasting triglyceride values less than 211 mg % are required within 3 months prior to randomization. Modification to the original protocol made during the year 1987 recommended a change in interim x-rays. Interim x-rays will only be taken on subjects noted to have DISH documented on the baseline visit (study entry) roentgenogram.

PRIOR AND CURRENT PROGRESS

Of the 135 original study participants, 122 remain in the study group. Deceased; 4, moved; 2, and dropped out; 7. All 122 active patients have now completed the 3 year drug intervention phase and no patients are currently on medication. Forty-four patients are being followed in the 2 year post-intervention phase which ends June 1991. Eighty-eight patients have completed the entire 5 year study. There were no cutaneous or noncutaneous adverse experiences during the past year. Benefits to the subjects are pending the completion of the research protocol.

CONCLUSIONS

No conclusions to date.

REPORT DATE: 08/01/91

WORK UNIT # 1809

DETAIL SUMMARY SHEET

TITLE: Investigation of Photosensitive Reactions to Piroxicam Via Topical Administration and Ultraviolet Light Exposure

KEYWORDS: piroxicam, photosensitivity, drug reaction

PRINCIPAL INVESTIGATOR: James, William LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Dermatology Service

STATUS: Completed
APPROVAL DATE: Jul 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This study is being done to define the ability of topically applied piroxicam ointment plus ultraviolet (UV) light to reproduce photosensitive drug eruptions.

TECHNICAL APPROACH

Once a patient is identified clinically as a probable reactor to piroxicam, photo patch testing using UVB and UVA alone and UVB and UVA with drug is accomplished.

PRIOR AND CURRENT PROGRESS

To date, seven patients have been tested. Three developed positive photo patch test reactions at the site of UVA piroxicam.

CONCLUSIONS

Approximately 50 percent of those tested have manifested photosensitivity to topical drug plan challenge. This may be a useful approach to confirm allergy without systemic challenge.

REPORT DATE: 03/05/91

WORK UNIT # 1810

DETAIL SUMMARY SHEET

TITLE: Evaluation of a Collagen Wound Dressing in Open Granulating Wounds

KEYWORDS: wound healing

PRINCIPAL INVESTIGATOR: Sperling, Leonard MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Dermatology Service

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare a new wound dressing for full thickness wounds (Helicote) with a conventional method (Telfa and Polysporin) on the healing (granulation and resurfacing) of full thickness wounds.

TECHNICAL APPROACH

Twenty patients will be selected for study. Ten will have their wounds treated with Helicote dressing (bovine collagen sponge with a semipermeable film backing). Ten will have their wounds treated with conventional wound care (Telfa and Polysporin) alone. Wounds will be assessed by tracing and photography, done at 1, 2, 4, 12, and 24 weeks.

PRIOR AND CURRENT PROGRESS

The decision has been made to terminate the study for the following reasons. The company making the product has been sold, the product has been discontinued, and all support for the study has been withdrawn. In addition, the trend in skin surgery has been to close wounds primarily. Finding suitable wounds for the study has been increasingly difficult, and no new, appropriate patients were found during the past year. Lastly, preliminary data show no difference between Helicote and controls. The results of the study would thus be "negative". It is, therefore, difficult to justify further patient participation, especially since appropriate wounds are proving to be rarely encountered.

CONCLUSIONS

Study should be terminated.

REPORT DATE: 04/24/91

WORK UNIT # 1811

DETAIL SUMMARY SHEET

TITLE: Evaluation of Antibiotic Induced Changes in the Microbial Flora of the External Ear

KEYWORDS: malignant otitis externa, microbial flora

PRINCIPAL INVESTIGATOR: Wakefield, Philip CPT MC

ASSOCIATES: James, William LTC MC

DEPARTMENT: Department of Medicine

SERVICE: Dermatology Service

STATUS: Ongoing

APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the hypothesis that antibiotics, both systemic and topical, change the flora of the external ear from a predominance of coagulase negative Staphylococcus toward gram negatives (especially Pseudomonas) in outpatients. Results may help identify risk factors for the development of malignant otitis externa following skin cancer surgery on the ear.

TECHNICAL APPROACH

Cultures of outpatient controls, acne, or rosacea patients, on chronic broad spectrum antibiotics and volunteers applying topical bacitracin to the external ear were performed as per the original protocol. Due to various problems, including the need for large bulky bandages and travel problems, we have not been able to recruit ear surgery patients for the protocol. The cultures of the 52 patients studied were negative. Because most Pseudomonas otitis externa occurs in adult diabetics, and in one study antibiotics increased ear Pseudomonas colonization in inpatients, it was felt that it would be more efficient to study this group first. Thus an amendment was submitted to study adult diabetics on antibiotics.

PRIOR AND CURRENT PROGRESS

Although the amendment to the above protocol was approved in October 1990, the primary investigator was on elective and thus unable to submit the required revisions until March 1991. Data collection will now begin.

CONCLUSIONS

No conclusions can be made as new data is not available. Collection of new data will now begin.

REPORT DATE: 09/30/91

WORK UNIT # 1812

DETAIL SUMMARY SHEET

TITLE: Oncogenes in Basal Cell Nevus Syndrome, Cowden's Disease and Tore's Disease

KEYWORDS: epidermal growth factor, EGF-R

PRINCIPAL INVESTIGATOR: Turiansky, George CPT MC

ASSOCIATES: Burman, Kenneth COL MC; Jones, William COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Dermatology Service

APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess whether there is a relationship between oncogenes and diseases involving multiple skin neoplasms associated with internal malignancies.

TECHNICAL APPROACH

DNA will be isolated from peripheral white blood cells and/or lesional tissue in study patients as per "Molecular Cloning: A Laboratory Manual" by T. Maniatis, et al. DNA samples will then be electrophoresed on agarose gel and hybridized with p32-labelled EGF-R probe after Southern blotting. Homologous areas will be visually assessed via autoradiograms. RNA samples will also be prepared by standard techniques and examined as above. No modifications noted to original protocol.

PRIOR AND CURRENT PROGRESS

Total number of subjects enrolled in last year is four, with 10 DNA samples sent from collaborators at Yale University. No patients have withdrawn from study, and no serious or unexpected adverse reactions have been noted.

CONCLUSIONS

A variant DNA band was noted after Southern blotting and probing with radio-labelled EGF-R in one affected and two unaffected family DNA samples of basal cell nevus syndrome patients. The significance of this finding will be further assessed by determining the specific base sequence of the DNA band (via polymerase chain reaction).

REPORT DATE: 06/26/91

WORK UNIT # 1813

DETAIL SUMMARY SHEET

TITLE: Pigmentary Patterns in Palmar, Plantar and Facial Skin and Nails; Their Incidence in the Adult Black Population

KEYWORDS: pigment patterns, nail bands, lentigenes

PRINCIPAL INVESTIGATOR: Malane, Susan MAJ MC

ASSOCIATES: James, William LTC MC; Furmanski, David DO

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Dermatology Service

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To survey the incidence of pigmentary patterns on the face, feet, hands, and nails in adult Black population to determine the incidence of facial patterned inherited lentigenes, focal acral hyperkeratosis and pigmented nail bands.

TECHNICAL APPROACH

Patients in the Dermatology and Outpatient Medicine Clinic will be asked for written consent. Their face, hands, and feet will be examined for the above findings.

PRIOR AND CURRENT PROGRESS

Approximately 300 patients were screened. Data is being compiled for possible publication.

CONCLUSIONS

Approximately 70% of adult Black patients screened had pigmented nail bands on at least one nail. Only one patient each was found with facial inherited lentigenes and focal acral hyperkeratosis.

REPORT DATE: 06/13/91

WORK UNIT # 1300-88

DETAIL SUMMARY SHEET

TITLE: Postoperative Evaluation of Patients with Differentiated Thyroid
Cancer: A Study Comparing ¹³¹I, ²⁰¹Tl and Magnetic Resonance Imaging
(MRI)

KEYWORDS: cancer, thyroid, scans

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC
ASSOCIATES: Neutze, Janet MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Jan 1988

FUNDING: Current FY: \$ 355 Previous FYs: \$ 2,400 Total: \$ 2,755

STUDY OBJECTIVE

To determine if thallium and magnetic resonance imaging (MRI) can effectively detect thyroid cancer.

TECHNICAL APPROACH

Patients with known thyroid cancer who are having thyroid scans for their routine care will also have a thallium scan and/or an MRI scan. These tests are compared to those results from Iodine ¹³¹I scans to determine if thallium is an effective agent.

PRIOR AND CURRENT PROGRESS

We have studied about 25 patients who have had thallium and/or MRI scans. We have shown that thallium and MRI are capable of detecting thyroid tumor that even ¹³¹I may not detect. Thus, we have incorporated these modalities into our routine patient care activities. There have been no adverse reactions or unexpected side effects. We want to keep this protocol active because we have an addendum approved to study pentavalent dimercapro-succinic acid (DMSA) with the same methodology.

CONCLUSIONS

MRI and thallium are helpful in patient care.

REPORT DATE: 06/13/91

WORK UNIT # 1302-88

DETAIL SUMMARY SHEET

TITLE: Cholestyramine Treatment of Thyrotoxicosis

KEYWORDS: cholestyramine, thyroid, thyrotoxicosis

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Solomon, Barbara DNSc; Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Mar 1988

FUNDING: Current FY: \$ 28 Previous FYs: \$ 15,348 Total: \$ 15,376

STUDY OBJECTIVE

To investigate the use of oral cholestyramine as a safe and rapid method of lowering serum thyroxine levels in hyperthyroid patients.

TECHNICAL APPROACH

We will use a randomized placebo crossover controlled design. Subjects will receive 4 grams cholestyramine powder four times a day or an equal amount of placebo powder for 14 days, no powders for 7 days, and then the reciprocal powder for 14 days. Serum T4 and T3 will be measured throughout each period.

PRIOR AND CURRENT PROGRESS

We have studied 16 patients and are now analyzing the data. We presented an abstract to the Endocrine Society in 1990 in which we noted that T4 and T3 levels were decreased further on cholestyramine than on control. We are analyzing the data and will submit it for publication shortly.

CONCLUSIONS

Cholestyramine is a useful adjunctive therapy for the early treatment of thyrotoxicosis.

REPORT DATE: 06/16/91

WORK UNIT # 1303-88

DETAIL SUMMARY SHEET

TITLE: The Clinical Application of In Situ Hybridization to Detect Viral Genomes and Oncogenes in Diseases of the Thyroid and Selected Viral Infections

KEYWORDS: virus, thyroid, probes

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Humphrey, Michael MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Apr 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if viral elements are important in thyroid disease.

TECHNICAL APPROACH

We shall use both Southern and Northern blots and in situ hybridization studies to determine if viruses are present in thyroid tissue from patients with various thyroid disorders. Polymerase chain reaction (PCR) and cloning techniques are also being employed.

PRIOR AND CURRENT PROGRESS

20 patients have been studied. We have been unable to find HIV-1 gene sequences in thyroid cell genomic DNA from patients with Graves' disease. We are continuing these lines of investigation and are presently using PCR to find p53 sequences in thyroid tissue.

CONCLUSIONS

Although HIV-1 sequences are lacking from thyroid tissue, we are actively pursuing the possibility that other viral genomes may be important in these disorders.

REPORT DATE: 06/11/91

WORK UNIT # 1306-88

DETAIL SUMMARY SHEET

TITLE: Predicting Energy Requirements in Women with Gestational Diabetes Mellitus (GDM)

KEYWORDS: energy, requirement, gestational diabetes

PRINCIPAL INVESTIGATOR: Coffey, Lauri MAJ SP

ASSOCIATES: Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare various methods of calculating or predicting energy expenditure in women with gestational diabetes mellitus (GDM). Indirect calorimetry will serve as the gold standard.

TECHNICAL APPROACH

Thirty females with gestational diabetes (Group A) will be recruited for the study. Pregnant women (Group B) will be measured during the third trimester: indirect calorimetry, dietary history, and anthropometric measures will be secured on each patient. Regression analysis will be utilized to analyze the data.

PRIOR AND CURRENT PROGRESS

Twenty-one patients have completed this study (three pregnant and 14 with GDM). Five pregnant patients with GDM dropped out of the study due to prenatal complications not associated with this study. All of the pregnant patients except two were in the last trimester of pregnancy. No adverse complications or benefits have been documented.

CONCLUSIONS

Conclusions have not been made since data collection is still ongoing.

REPORT DATE: 03/18/91

WORK UNIT # 1308-88

DETAIL SUMMARY SHEET

TITLE: Serum Cholesterol Antibodies

KEYWORDS: cholesterol, antibodies

PRINCIPAL INVESTIGATOR: Seiken, Gail CPT MC

ASSOCIATES: Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,520 Total: \$ 1,520

STUDY OBJECTIVE

To determine if patients with various diseases have autoantibodies against cholesterol.

TECHNICAL APPROACH

Antibodies against cholesterol are measured by ELISA techniques. The titer of these antibodies are measured and quantitated and compared in various patient groups.

PRIOR AND CURRENT PROGRESS

Dr. Seiken was not able to continue these studies.

CONCLUSIONS

None.

REPORT DATE: 03/18/91

WORK UNIT # 1309-88

DETAIL SUMMARY SHEET

TITLE: Alterations of Thyroidal Iodine Release During Atrial Natriuretic Factor (ANF) Infusions in Hyperthyroid Subjects

KEYWORDS: ANF, iodine, hyperthyroidism

PRINCIPAL INVESTIGATOR: Peele, Mark CPT MC

ASSOCIATES: Wartofsky, Leonard COL MC; Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 3,430 Previous FYs: \$ 11,846 Total: \$ 15,276

STUDY OBJECTIVE

To study the effects of atrial natriuretic peptide (ANP) on thyroidal iodine release and peripheral iodine metabolism during thyrotoxicosis.

TECHNICAL APPROACH

Thyrotoxic volunteers receive radioiodine to label the thyroidal iodine pool (¹³¹I) and the peripheral iodine pool (¹²⁵I). The metabolic turnover of the peripheral and thyroidal iodine pools is determined by activity measurements of aliquot of sera and plotted against time. The infusion of exogenous ANP during the period of peripheral and total iodine metabolic turnover determinations allows measurement of alterations in iodine metabolism or release during ANP infusions.

PRIOR AND CURRENT PROGRESS

The study was closed by the Department Chief, COL Leonard Wartofsky. The Principal Investigator is no longer at WRAMC.

CONCLUSIONS

None.

DETAIL SUMMARY SHEET

TITLE: Effects of Sodium, Calcium and pH Fluxes on Prolactin Secretion in a Rat Pituitary Cell Line

KEYWORDS: prolactin, GH3, calcium

PRINCIPAL INVESTIGATOR: Galloway, Richard MAJ MC

ASSOCIATES: Smallridge, Robert COL MC; Fein, Henry LTC MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 10,649 Total: \$ 10,649

STUDY OBJECTIVE

To study the effect of changes in cytoplasmic calcium and sodium ion concentrations on prolactin secretion in GH3 cells.

TECHNICAL APPROACH

Ion specific, membrane permeable, fluorescent dyes are loaded into the cell cytoplasm. The fluorescence of a cell suspension is measured in a PTI Deltascan Spectrofluorimeter and quantitated. Intracellular sodium, calcium, or pH is then manipulated with the use of channel agonist or antagonists, and the effect of these manipulations on cytoplasmic ion concentration and prolactin secretion is measured. The toxin, monensin, is an important tool in these manipulations.

PRIOR AND CURRENT PROGRESS

Monensin produces dose-related increases in cytosolic pH and sodium which are dependent upon external Na^+ . The increase in cytosolic calcium is more complex. While a membrane $\text{Na}^+/\text{Ca}^{2+}$ exchanger is involved, monensin was shown to mobilize calcium from an intracellular storage site separate from the TRH releasable pool. Monensin decreases prolactin secretion in a dose response manner but at a lower concentration than required to effect ion changes.

CONCLUSIONS

(1) GH3 cells possess a $\text{Na}^+/\text{Ca}^{2+}$ exchanger; (2) Monensin increases cytoplasmic calcium from both intra- and extracellular sources but not primarily via the $\text{Na}^+/\text{Ca}^{2+}$ exchanger; (3) Calcium influx in response to monensin is not through L-type Ca^{2+} channels; (4) Monensin regulates an intracellular releasable calcium pool distinct from that of TRH or ionomycin.

REPORT DATE: 03/11/91

WORK UNIT # 1311-88

DETAIL SUMMARY SHEET

TITLE: Incidence of Fractures in Post-Menopausal Women

KEYWORDS: fractures, thyroid hormone, post-menopausal

PRINCIPAL INVESTIGATOR: Solomon, Barbara DNSc

ASSOCIATES: Wartofsky, Leonard COL MC; Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether having thyroid disease or taking thyroid hormone is a risk factor for fractures in post-menopausal women.

TECHNICAL APPROACH

Data will be collected via survey.

PRIOR AND CURRENT PROGRESS

Two hundred and twenty-seven interviews out of a required 500 interviews have been completed to date. Due to detail to Acting Head Nurse on Ward 47, no work on this protocol has been done since December 1990. It is anticipated that the delay in collecting interviews will continue until at least June 1991.

CONCLUSIONS

None.

REPORT DATE: 05/16/91

WORK UNIT # 1312-89

DETAIL SUMMARY SHEET

TITLE: Treatment of Oligospermia with Antiestrogens

KEYWORDS: oligospermia, clomiphene, tamoxifen

PRINCIPAL INVESTIGATOR: Glass, Allan COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 737 Total: \$ 737

STUDY OBJECTIVE

To compare the effectiveness of tamoxifen and clomiphene in treating oligospermia.

TECHNICAL APPROACH

Randomized, prospective study of clomiphene, 25 mg every other day, and tamoxifen, 10 mg twice daily, for treatment of idiopathic oligospermia.

PRIOR AND CURRENT PROGRESS

Ten patients recruited; none have completed the protocol. No side effects. No publications.

CONCLUSIONS

Deferred.

REPORT DATE: 06/16/91

WORK UNIT # 1313-89

DETAIL SUMMARY SHEET

TITLE: The Influence of Prolonged Polar Residence Upon Cellular Receptors: The Environmental Genome Interaction

KEYWORDS: cold, thyroid, polar

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 825 Previous FYs: \$ 10,521 Total: \$ 11,346

STUDY OBJECTIVE

To determine the changes in thyroid hormone kinetics and action in the cold.

TECHNICAL APPROACH

Labelled and unlabelled hormones will be given and kinetics determined.

Binding studies will also be performed.

PRIOR AND CURRENT PROGRESS

The only portions of this study that we have been able to perform relate to those initiated by Dr. Reed at the National Naval Medical Center, Bethesda, MD. Although this protocol was approved by DCI, funding was not approved by the Combat Casualty Care Research Program. Despite the fact that this protocol is mission oriented and is designed to understand a mission related subject (i.e., how soldiers adapt to cold environments) and also despite the fact that R & D requested protocols be submitted, this protocol has not been approved at R & D. COL Slaughter in his letter of 09 Mar 90 to me says "your experience as a researcher makes you rather overqualified for this program. I remain surprised that you continue to seek financial support..."

CONCLUSIONS

No scientific conclusions yet.

REPORT DATE: 06/11/91

WORK UNIT # 1314-89

DETAIL SUMMARY SHEET

TITLE: The Efficacy of Iodine Restricted Diets in the Treatment of Thyroid Cancer

KEYWORDS: iodine restriction, thyroid, cancer

PRINCIPAL INVESTIGATOR: Coffey, Lauri MAJ SP

ASSOCIATES: Burman, Kenneth COL MC; Solomon, Barbara DNSc

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This study seeks to determine whether the iodine restricted diet (IRD) prescribed at WRAMC increases radioiodine uptake and visualization of thyroid tissue or metastatic lesions in patients following thyroidectomy for thyroid cancer.

TECHNICAL APPROACH

Forty-five thyroid cancer patients will be recruited to participate in this placebo controlled (regular diet) crossover (low iodine diet) study design. This study randomizes the order of treatment assignment and is a multi-variate randomized block (repeated measures of crossover design) analysis of covariance.

PRIOR AND CURRENT PROGRESS

Nineteen patients have completed the study. There have been no adverse effects experienced. The patients have not received any direct benefits from their participation.

CONCLUSIONS

Preliminary evidence indicates that patients can comply with the low iodine diet as documented from urinary iodine excretion. It appears that the low iodine diet has clinical utility in selected patients.

REPORT DATE: 08/08/91

WORK UNIT # 1315-89

DETAIL SUMMARY SHEET

TITLE: Serum Lipids, Lipoproteins and Apoproteins in Patients with Long Term Corticosteroid Exposure

KEYWORDS: lipids, lipoprotein, corticosteroid

PRINCIPAL INVESTIGATOR: Chamberlain, Bruce CPT MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 560 Total: \$ 560

STUDY OBJECTIVE

To determine the effects of chronic corticosteroid exposure on plasma lipids, lipoproteins, and apoproteins in patients with steroid dependent asthma and chronic obstructive pulmonary disease (COPD).

TECHNICAL APPROACH

Study subjects are identified through referral and record review. Once identified, they fill out a questionnaire which reviews diet, lifestyle, and medical history. Blood samples are then drawn for serum lipids and apoproteins, as well as other relevant labs to rule out secondary causes of hyperlipidemia. Medical records are then reviewed to assess activity of the underlying condition and cumulative steroid exposure.

PRIOR AND CURRENT PROGRESS

To date, data has been collected on five patients. However, because the principal investigator has been transferred from Walter Reed Army Medical Center, request that this study be terminated.

CONCLUSIONS

No conclusions can be drawn from the data collected so far. Due to lack of patient participation and the transfer of the PI, this study should be closed.

REPORT DATE: 07/23/91

WORK UNIT # 1316-89

DETAIL SUMMARY SHEET

TITLE: Identification of Unique Nucleotides in the Thyroid Gland of Patients with Various Thyroid Disorders

KEYWORDS: thyroid, genes, RNA

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Nagy, Endre MD

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 5,006 Total: \$ 5,006

STUDY OBJECTIVE

To identify unique thyroid genes that are expressed in autoimmune thyroid disease and cancer.

TECHNICAL APPROACH

Construct cDNA library from thyroid tissue of patients with autoimmune thyroid disease and cancer. The cDNA library is then screened by labelling RNA or cDNA from the tissue of interest.

PRIOR AND CURRENT PROGRESS

We have been successful in identifying several unique clones from patients with autoimmune thyroid disease. These clones have been sequenced, and we have divided them into three categories. One group is related to NADH dehydrogenase, one group to thyroglobulin, and one group remains heretofore undescribed previously.

CONCLUSIONS

Thyroid disease is associated with the translation of unique proteins that may be important in modulating cellular growth.

REPORT DATE: 08/08/91

WORK UNIT # 1317-89

DETAIL SUMMARY SHEET

TITLE: Self Efficacy Beliefs and Diabetes Management Survey

KEYWORDS: diabetes, self-efficacy, self-care

PRINCIPAL INVESTIGATOR: Duncan, William LTC MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the influence of diabetes self-efficacy beliefs on the self-care behaviors of adults diagnosed within 3 years with noninsulin-dependent diabetes mellitus.

TECHNICAL APPROACH

Diabetic patients will be evaluated initially and 3 months later with the following instruments: Insulin Management Diabetes Self-Efficacy Scale, Insulin Management Diabetes Health Belief Scale, Insulin Management Diabetes Self-Care Scale, Diabetes Care Profile.

PRIOR AND CURRENT PROGRESS

Forty-five subjects have completed the 3 month protocol. We have asked for and received permission to expand the criteria for inclusion in this study. An additional 15 patients have been enrolled. To date, 30 subjects have completed the 1-year protocol.

CONCLUSIONS

Self-efficacy beliefs about diabetes mellitus predicted 64% of the diabetes self-care behaviors after 3 months. The addition of health beliefs accounted for 8% of self-care behavior after 3 months.

REPORT DATE: 08/16/91

WORK UNIT # 1318-90

DETAIL SUMMARY SHEET

TITLE: The Lipids Effects of Continuous Vs. Sequential Conjugated Equine
Estrogen and Medroxyprogesterone Acetate Therapy in Postmenopausal
Women

KEYWORDS: lipids, estrogen, progesterone

PRINCIPAL INVESTIGATOR: Burch, Henry MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Completed
APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare the lipid effects of a newer estrogen/progesterone regimen to
conventional estrogen/progesterone therapy.

TECHNICAL APPROACH

No patients completed protocol.

PRIOR AND CURRENT PROGRESS

Because it was extremely difficult to find study participants, and the two
associate investigators PCS'd, the study is being closed.

CONCLUSIONS

None.

REPORT DATE: 11/20/91

WORK UNIT # 1319-90

DETAIL SUMMARY SHEET

TITLE: Alterations of Water and Electrolyte Metabolism During Hypothyroidism:
Effect of Atrial Natriuretic Peptide Infusion

KEYWORDS: water, thyroid

PRINCIPAL INVESTIGATOR: Peele, Mark CPT MC

ASSOCIATES: Wartofsky, Leonard COL MC; Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To measure salt and water metabolism in hypothyroid subjects.

TECHNICAL APPROACH

Infusions of antinuclear factor (ANF) are given to assess effects of water excretion.

PRIOR AND CURRENT PROGRESS

No patients were admitted to protocol as Dr. Peele was posted to another hospital.

CONCLUSIONS

None.

REPORT DATE: 09/12/91

WORK UNIT # 1320-90

DETAIL SUMMARY SHEET

TITLE: Evaluation of Pathological and Normal Thyroid Tissue for the Presence of Retroviral Genomic Nucleotides

KEYWORDS: thyroid, retroviral, HIV

PRINCIPAL INVESTIGATOR: Humphrey, Michael MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 3,304 Previous FYs: \$ 0 Total: \$ 3,304

STUDY OBJECTIVE

To use molecular biology techniques to identify, purify and sequence retroviral gene sequences located within thyroid tissue.

TECHNICAL APPROACH

Utilization of agarous gel electrophoresis for separation of genomic DNA isolated from Graves' thyrocytes. Followed by Southern transfer to nylon filters and DNA hybridization using HIV specific probes. The polymerase chain reaction (PCR) was also used in an attempt to amplify retroviral sequences from DNA isolated from thyrocytes.

PRIOR AND CURRENT PROGRESS

Over the last 2 years, we have been unable to confirm the presence of HIV-1-related gene sequences in thyroid genomic DNA or DNA isolated from WBC's of Graves' patients. DNA hybridization and PCR studies were performed on genomic material isolated from 15 patients; all studies failed to detect HIV-1-related sequences. Current efforts are considering other types of retroviral agents as having possible etiologic roles in Graves' disease.

CONCLUSIONS

We were unable to confirm the existence of HIV-1-related DNA sequences in Graves' specimens.

REPORT DATE: 08/14/91

WORK UNIT # 1321-90

DETAIL SUMMARY SHEET

TITLE: Processing of Atrial Natriuretic Peptide (ANP) and Its Receptor on Cultured Human Thyroid Cells: Effect of Thyroid Stimulating Hormone

KEYWORDS: ANP, thyroid, TSH

PRINCIPAL INVESTIGATOR: Tseng, Yueh-Chu PhD

ASSOCIATES: Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$12,689 Previous FYs: \$ 0 Total: \$ 12,689

STUDY OBJECTIVE

To trace the atrial natriuretic peptide (ANP) processing pathway after its binding to thyroid membrane, and to investigate the effect of thyroid stimulating hormone (TSH) on the processing of ANP in thyroid cells.

TECHNICAL APPROACH

Surgically removed thyroid gland tissue from patients with thyroid diseases will be used to initiate tissue culture for study. [125I]-ANP will be incubated with cells at 4 degrees C for 2 hours. After washing to remove exogenous ANP, cells will be incubated with fresh media in the absence or presence of TSH at 37 degrees C over specific time periods. Radioactivities recovered on cell surface membrane, inside the cells, and in media will be determined to trace the ANP processing pathway. [125I] ANP and its metabolites in media will be analyzed by HPLC.

PRIOR AND CURRENT PROGRESS

After incubation at 4 degrees C for 2 hours, [125I]-ANP bound to surface membrane could not be competitively displaced by excess ANP during subsequent incubation at 37 degrees C, indicating that internalization immediately followed ANP-receptor complex formation. Pretreatment of cells with chloroquine (CQ) caused significant increases in internalized ANP and decreases in radioactivity recovered in incubation media, suggesting mediation of ANP-receptor complex processing via CQ-sensitive lysosomal enzymes. The rate of ANP-receptor complex internalization was stimulated by TSH.

CONCLUSIONS

In cultured human thyroid cells, receptor bound ANP will be internalized and processed by lysosomal enzymes. The internalization rate is stimulated by incubation of cells with TSH.

REPORT DATE: 08/27/91

WORK UNIT # 1322-90

DETAIL SUMMARY SHEET

TITLE: Treatment of Impotence in Diabetic Men

KEYWORDS: impotence, diabetes, yohimbine

PRINCIPAL INVESTIGATOR: Humphrey, Michael CPT MC

ASSOCIATES: Glass, Allan LTC MC

DEPARTMENT: Department of Medicine

SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 427 Previous FYs: \$ 0 Total: \$ 427

STUDY OBJECTIVE

To compare the effectiveness, acceptance, and complication rate of an externally applied vacuum device versus yohimbine for the treatment of impotence in the diabetic male population, and to identify any specific characteristics of patients who respond favorably to each therapy.

TECHNICAL APPROACH

Diabetic men presenting to the Endocrine Clinic will be screened to determine the status of erectile function. All subjects with erectile dysfunction will be offered participation. Evaluation will consist of history and physical, routine and endocrine lab testing, and urologic consultation. Testing will be conducted in 3-month phases with yohimbine and Erec-Aid. Initial form of therapy will be randomized with a 3-month washout period between therapeutic periods. The only protocol change involves the urologic examination, which is generally being conducted on an outpatient rather than inpatient basis.

PRIOR AND CURRENT PROGRESS

Thus far, 14 patients have been entered into the study, with an ultimate goal of 58. Eight patients have completed or nearly completed the protocol. No significant or untoward complications have occurred from either therapeutic modality. Although results remain preliminary, thus far use of Erec-Aid has proven effective and well tolerated in the majority of patients. On the other hand, yohimbine has resulted in little improvement.

CONCLUSIONS

Due to my absence, recruitment into this protocol has decreased over the last 6 months. Active recruitment will resume immediately. Thus far, Erec-Aid therapy appears effective and well tolerated in the majority of patients.

REPORT DATE: 08/13/91

WORK UNIT # 1324-90

DETAIL SUMMARY SHEET

TITLE: Use of Corticotropin Release Hormone in the Evaluation of
Hypocortisolemia and Hypercortisolemia

KEYWORDS: hypercortisolemia, hypocortisolemia, Cushing's syndrome

PRINCIPAL INVESTIGATOR: Schaaf, Marcus MD

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define source of excessive ACTH production in ACTH-dependent Cushing's syndrome (pituitary or ectopic), and to help in differentiating other temporary hypercortisolemic states, such as depression. Additionally, hypocortisolemic patients with low ACTH values will be examined, to distinguish hypothalamic versus pituitary cause.

TECHNICAL APPROACH

Corticotropin-releasing hormone (CRH) 1.0 ug/kg will be administered over 1 to 2 minutes into a peripheral vein with peripheral venous blood sampling for ACTH and cortisol at -15, -1, +5, +15, +30 and +60 minutes. When CRH is administered during inferior petrosal sinus (IPS) sampling for localization of pituitary ACTH-secreting tumors, blood from both right and left sinuses and a peripheral vein will be sampled at 3, 5 and 10 minutes after CRH.

PRIOR AND CURRENT PROGRESS

Only one patient with untreated Cushing's syndrome was encountered during the past year. In this patient, CRH administration during IPS sampling correctly identified and lateralized an ACTH-secreting adenoma which was successfully removed. There was no adverse reaction. No hypocortisolemic patients were treated.

CONCLUSIONS

CRH administration during IPS sample is the most reliable and sensitive way to identify and localize pituitary ACTH-secreting tumors in Cushing's syndrome. It should be performed before pituitary surgery in such patients.

REPORT DATE: 08/12/91

WORK UNIT # 1325-90

DETAIL SUMMARY SHEET

TITLE: Physiologic Determinants of Exercise Capacity in Hyperthyroidism

KEYWORDS: hyperthyroidism, exercise

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Completed
APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the metabolic changes in hyperthyroidism.

TECHNICAL APPROACH

Perform metabolic tests during exercise in volunteers with hyperthyroidism. Muscle biopsies are also studied for enzymatic changes.

PRIOR AND CURRENT PROGRESS

This project was not approved for funding by VA-DOD for reasons other than the scientific relevance and importance of this project. Dr. Martin, our collaborator at Washington University in St. Louis, has continued to perform portions of these studies, but the aspects we were going to perform have not been performed due to lack of personnel funds for this project. Therefore, this study is being closed at this time.

CONCLUSIONS

None.

REPORT DATE: 11/04/91

WORK UNIT # 1327-90

DETAIL SUMMARY SHEET

TITLE: Mechanism of Tumor Necrosis Factor Effects of Thyroid Cells

KEYWORDS: tumor necrosis factor, thyroid function

PRINCIPAL INVESTIGATOR: Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To examine the role of tumor necrosis factor (TNF) in altering thyroid function.

TECHNICAL APPROACH

Human cultured cells will be exposed to TNF. Alterations in cyclic nucleotide and thyroglobulin secretion will be noted.

PRIOR AND CURRENT PROGRESS

This study was completed and a manuscript published in Thyroid.

CONCLUSIONS

TNF inhibits TSH stimulation of thyroid cells and probably plays a role in the sick euthyroid syndrome.

REPORT DATE: 03/18/91

WORK UNIT # 1349-84

DETAIL SUMMARY SHEET

TITLE: Immunoglobulin Production in Thyroid Disease

KEYWORDS: immunoglobulin, production, thyroid

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Wartofsky, Leonard COL MC; Nagy, Endre MD

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Nov 1983

FUNDING: Current FY: \$ 903 Previous FYs: \$ 18,471 Total: \$ 19,374

STUDY OBJECTIVE

To: 1) document presence and frequency of anti-receptor antibodies in patients with autoimmune thyroid disease; 2) culture lymphocytes of these patients and measure specific antibodies generated; 3) document presence and frequency of anti-idiotypic antibodies in these diseases; 4) document and measure frequency of immune complexes in patients' serum; 5) generate anti-receptor and anti-idotypic antibodies in animals; and 6) analyze immune parameters in postpartum thyroiditis.

TECHNICAL APPROACH

Use ELISA techniques to measure specific antibodies against TSH, TSH receptor or thyroglobulin. Lymphocytes are isolated on Ficoll-hypaque by separation procedures, and specific antibodies are measured by ELISA immune complex or by specific binding to C3B by ELISA. We will also use the cloned TSH receptor protein in these studies.

PRIOR AND CURRENT PROGRESS

We have determined that approximately 20% of patients with autoimmune thyroid disease have circulating antibodies against insulin and against TSH. We believe each of these antibodies are anti-idiotypic in nature. We have isolated intrathyroidal B cells from several patients and have determined that the B cells are capable of making a wide variety of antibodies against TSH receptor, TSH, insulin, Beta receptor and microsome, as well as TSH receptor antibody. These are new studies that have not been published by other groups. We have utilized a C3B binding assay to measure that immune complexes occur in about 50% of patients with Graves' disease, and we have disrupted these immune complexes to indicate that there are TSH binding anti-idiotypes and TSH receptor antibodies combined in some of these immune complexes.

CONCLUSIONS

Autoimmune thyroid disease is a wide-ranging disease in which a panoply of antibodies are formed, not just against TSH receptor, but against TSH, microsomes, thyroglobulin, insulin, and beta receptors.

REPORT DATE: 03/13/91

WORK UNIT # 1351-84

DETAIL SUMMARY SHEET

TITLE: Cyclosporin Treatment of Graves' Ophthalmopathy

KEYWORDS: cyclosporine, exophthalmos, Graves' disease

PRINCIPAL INVESTIGATOR: Wartofsky, Leonard COL MC

ASSOCIATES: Ahmann, Andrew MAJ MC; LaPiana, Francis COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Jan 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 538 Total: \$ 538

STUDY OBJECTIVE

To assess the effectiveness of cyclosporine in the treatment of severe Graves' ophthalmopathy.

TECHNICAL APPROACH

Patients with severe Graves' ophthalmopathy demonstrating some progression in the prior year are randomized to receiving cyclosporine or high dose prednisone for 3 weeks. There is then a 3 week rest period before crossover to the alternative drug for 3 weeks. Objective improvement is assessed by measurement of proptosis, tonometry, ATA ophthalmopathy index, and serial orbital CT scans.

PRIOR AND CURRENT PROGRESS

Eight patients have been entered into the study. We are hopeful that the data will be analyzed and a manuscript written when and if an additional four to eight subjects can be recruited. The prevalence of significant ophthalmopathy accompanying Graves' disease appears to have declined.

CONCLUSIONS

None as yet.

REPORT DATE: 07/15/91

WORK UNIT # 1356-84

DETAIL SUMMARY SHEET

TITLE: Ketoconazole-Induced Suppression of Serum Testosterone Levels in Men

KEYWORDS: ketoconazole, testosterone, gonadotropins

PRINCIPAL INVESTIGATOR: Glass, Allan LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Jul 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 4,352 Total: \$ 4,352

STUDY OBJECTIVE

To determine whether the stimulation of serum LH and FSH that follows the ketoconazole-induced reduction in serum testosterone is useful as a test of pituitary gonadotropin reserve.

TECHNICAL APPROACH

Subjects are given ketoconazole 200 mg every 8 hours for 7 days, and serum LH, FSH, testosterone, and 17-OH-progesterone are measured before and after drug administration.

PRIOR AND CURRENT PROGRESS

No new patients were studied during the last 12 months. During previous periods, normal subjects and a small number of patients with hypothalamic-pituitary disorders were evaluated.

CONCLUSIONS

Ketoconazole lowers serum testosterone levels and stimulates serum LH and FSH levels in normal men. The response of patients with hypothalamic-pituitary disorders is not established due to the small number of subjects studied.

REPORT DATE: 04/03/91

WORK UNIT # 1359-85

DETAIL SUMMARY SHEET

TITLE: Newer Investigations into the Immune Mechanisms of Thyroid Disease
(1985)

KEYWORDS: immunology, thyroid disease

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Baker, James MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Feb 1985

FUNDING: Current FY: \$ 410 Previous FYs: \$ 49,718 Total: \$ 50,128

STUDY OBJECTIVE

To define the T and B cell abnormalities in patients with thyroid disease, both in the peripheral mononuclear cells, as well as in the intra-thyroidal mononuclear cells.

TECHNICAL APPROACH

There are various aspects of this study: 1) Peripheral mononuclear cells are isolated and cultured in the presence of antigen specific and non-specific stimuli; 2) Similar studies are performed with intra-thyroidal cells; 3) Genes encoding unique or interesting cellular proteins are characterized; and 4) Antigen-specific proteins are characterized.

PRIOR AND CURRENT PROGRESS

We have isolated clones of cells and are studying their antigen specific characteristics. We will try to make hybridomas against interesting proteins, and we have shown that viral elements do not seem to be present. We have demonstrated that the genetic response is polyclonal in nature. ANP, lymphokines, and EGF are important in mediating thyroid responses in autoimmune disorders.

CONCLUSIONS

Graves' disease is an autoimmune disease in which there is a heterogeneous activation of T and B cells. We shall continue to analyze the genetic responses of interest.

REPORT DATE: 08/08/91

WORK UNIT # 1361-85

DETAIL SUMMARY SHEET

TITLE: 1,25-Dihydroxyvitamin D Action at the Nuclear Level

KEYWORDS: 1,25-Dihydroxyvitamin D, liver, endocrine

PRINCIPAL INVESTIGATOR: Duncan, William LTC MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: May 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 80,475 Total: \$ 80,475

STUDY OBJECTIVE

To identify proteins synthesized by the liver in response to 1,25(OH)2D3 treatment.

TECHNICAL APPROACH

The technique of differential hybridization will be used to enrich the poly A-mRNA prior to cell free translation. PCR technology will also be utilized to determine if the vitamin D receptor is present in liver.

PRIOR AND CURRENT PROGRESS

Techniques to conduct this research protocol have been developed to include isolation of hepatic mRNA and Northern analysis, and the rearing of vitamin D deficient rats for the first time at WRAMC. Using the polymerase chain reaction (PCR) methodology we have detected the vitamin D receptor in rat liver and a human hepatoma cell line (Hep G2). We are currently attempting to develop a quantitative PCR technique for this receptor.

CONCLUSIONS

This protocol is central to our effort to understand the molecular basis of vitamin D action. The vitamin D receptor is present in the liver.

REPORT DATE: 08/08/91

WORK UNIT # 1363-85

DETAIL SUMMARY SHEET

TITLE: 1,25-Dihydroxyvitamin D Receptors in Liver and Skeletal Muscle

KEYWORDS: 1,25-dihydroxyvitamin D, liver, muscle

PRINCIPAL INVESTIGATOR: Duncan, William LTC MC

ASSOCIATES: Wray, H. Linton COL MC

DEPARTMENT: Department of Medicine

SERVICE: Endocrine-Metabolic Service

STATUS: Completed

APPROVAL DATE: Jul 1985

FUNDING: Current FY: \$ 1,096 Previous FYs: \$ 13,475 Total: \$ 14,571

STUDY OBJECTIVE

To identify 1,25(OH)2D3 receptors in rat liver and to study the regulation of this receptor.

TECHNICAL APPROACH

Standard biochemical techniques for identification will be employed after isolation of rat liver nuclei.

PRIOR AND CURRENT PROGRESS

The 1,25(OH)2D3 receptor has been identified and characterized in rat liver nuclei. In addition, using polymerase chain reaction (PCR) methodology, we have identified the mRNA for this receptor in rat liver and in a human hepatoma cell line. The receptor has been identified in skeletal muscles, so no further work has been done with muscles. We have studied the regulation of this receptor by estradiol and triiodothyronine and have found differences in both hormones. The regulation of this receptor by these hormones also differs in the tissues we have studied (liver, kidney, intestine).

CONCLUSIONS

The vitamin D receptor is present in liver. The hormonal regulation of this receptor is complex. Several hormones regulate this receptor in an organ-specific manner.

REPORT DATE: 03/18/91

WORK UNIT # 1367-86

DETAIL SUMMARY SHEET

TITLE: Modification of Diabetogenic Effects of Pentamidine

KEYWORDS: modification, diabetogenic, pentamidine

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Completed
APPROVAL DATE: Oct 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 7,181 Total: \$ 7,181

STUDY OBJECTIVE

To determine the effects of pentamidine on serum glucose and insulin and pancreatic insulin in rats injected with this agent.

TECHNICAL APPROACH

Male rats weighing 150-250 grams will be obtained and placed on water ad lib as noted. Following 5 days of observation, rats will be divided into 5 groups. The rats will receive daily intraperitoneal injections for 14 days as follows: Group 1 - sterile water, Group 2 - 4 mg/kg of pentamidine, Group 3 - 8 mg/kg of pentamidine, Group 4 - 16 mg/kg pentamidine, and Group 5 - 24 mg/kg pentamidine. Every 17 hours, the rats will be weighed, fasted for 2 hours, and have blood glucose measured. After day 14, rats will be fasted overnight but given water. Next morning they will be weighed, and glucose is again checked.

PRIOR AND CURRENT PROGRESS

Insulin over glucose ratio was 3.4 in the group that received 14 days sterile water, and it rose to 1.47 in the group that received 4 mg/kg pentamidine and to 1.0 in the groups that received 16 mg/kg pentamidine. These studies have been repeated with approximately the same results. Preliminary histologic exam of the pancreas indicate an increased insulin content in the pancreas in the pentamidine treated rats. These results taken together indicate that pentamidine has a significant effect of lowering insulin secretion and allowing elevated glucose. The mechanism of this seems to be that, although pentamidine is synthesized, the pancreas is unable to secrete it. Further research is proceeding by repeating these studies and by in vitro culture techniques that Dr. Hays is performing at NAMRI in Bethesda, MD.

CONCLUSIONS

Pentamidine works to inhibit insulin secretion.

REPORT DATE: 03/04/91

WORK UNIT # 1369-86

DETAIL SUMMARY SHEET

TITLE: Magnesium Status and Thyroid Disease

KEYWORDS: magnesium, thyroid, disease

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Oct 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 4,353 Total: \$ 4,353

STUDY OBJECTIVE

To measure magnesium and zinc levels in blood, tissue, and urine in control patients and in patients with hyperthyroidism and hypothyroidism.

TECHNICAL APPROACH

Plasma magnesium and zinc, red blood cell magnesium and zinc, mononuclear cell magnesium and zinc content and 24 hour urine excretion of magnesium and zinc were measured. Red blood cell and white blood cell counts were determined on a counter model ZM, and hemoglobin was measured with a counter electronics hemoglobinometer. Whole blood was hemolyzed by dilution with deionized water, vortexed, and then frozen. Plasma for heparinized tubes was separated from whole blood by centrifugation and frozen for later analysis. Mononuclear cells were isolated by ISOLYMPH, with harvesting and counting of the cells followed by lysis with deionized water and ultrasonication to release magnesium and zinc.

PRIOR AND CURRENT PROGRESS

Twenty-five controls, (10 men and 15 women), 11 hyperthyroid and 29 hypothyroid patients volunteered to participate in this study. Magnesium status results indicated that although there was a tendency for patients with hyperthyroidism to have lower plasma concentration of magnesium, as compared to hypothyroid and euthyroid subjects, the differences were not significant. Similarly, red blood cell magnesium did not differ between the groups. No significant association between blood cell magnesium and any tests of thyroid function was noted. There was a significant negative correlation between plasma magnesium and resin T3 uptake ($r = -0.42$; $P < 0.01$). In contrast to red blood cell and plasma magnesium, urinary excretion and urinary clearance of magnesium were significantly lower in hypothyroid patients as compared to both hyperthyroid and euthyroid subjects.

CONCLUSIONS

Plasma magnesium concentrations tended to be lower in hyperthyroid patients, but differences among the groups were not significant. Similarly, red blood cell concentration and mononuclear cell content of magnesium did not differ among the three groups. In contrast, hypothyroid patients showed marked decreases in urinary magnesium excretion as compared to hyperthyroid and euthyroid subjects.

REPORT DATE: 03/21/91

WORK UNIT # 1371-86

DETAIL SUMMARY SHEET

TITLE: Transplantation Antigens on Spermatozoa

KEYWORDS: transplantation, HLA, spermatozoa

PRINCIPAL INVESTIGATOR: Glass, Allan COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Nov 1985

FUNDING: Current FY: \$ 3,747 Previous FYs: \$ 6,958 Total: \$ 10,705

STUDY OBJECTIVE

To determine the nature and amount of transplantation antigens in spermatozoa.
To compare transplantation antigens in blood cells and sperm.

TECHNICAL APPROACH

Detection of transplantation antigens in spermatozoa by use of specific antisera and fluorescent detection techniques. Detection of released antigens by means of hemolytic plaque assay.

PRIOR AND CURRENT PROGRESS

In previous years, we showed that sperm did not express HLA antigens on their surface. This year, to explore other possibilities of identifying sperm, we examined whether sperm had messenger RNA, which might indicate protein synthesis. Our result showed no mRNA in sperm. As a pilot project to see if DNA could be used to identify sperm, we used a Y-chromosome-specific DNA probe to identify Y-chromosome containing sperm; this was successful. A published method of separating X- and Y-containing sperm was examined using in situ hybridization with the Y-specific DNA probe; the technique did not affect the percentage of Y-containing sperm. Further studies will be aimed at identifying and selecting sperm according to DNA composition (this is still in a very preliminary stage).

CONCLUSIONS

Sperm do not express HLA antigens on their surface. Sperm do not contain measureable messenger RNA, implying that they probably synthesize very little protein. Consequently, it seems unlikely that individual sperm could be characterized by protein constituents. The presence of Y-chromosome in sperm can be determined by in situ hybridization with a DNA probe.

REPORT DATE: 03/21/91

WORK UNIT # 1372-86

DETAIL SUMMARY SHEET

TITLE: Effect of Altered Energy Balance on Sexual Maturation in Rats

KEYWORDS: energy balance, sexual maturation, hyperthyroidism

PRINCIPAL INVESTIGATOR: Glass, Allan COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Nov 1985

FUNDING: Current FY: \$ 3,124 Previous FYs: \$ 61,131 Total: \$ 64,255

STUDY OBJECTIVE

To determine the effect of alterations in energy balance on sexual maturation in rats.

TECHNICAL APPROACH

Manipulation of energy balance in rats by food restriction, hyperthyroidism, or catecholamine infusion. Parameters of puberty and growth monitored serially, including assessment of such factors as hormone levels, growth rates, timing of vaginal opening, and sperm production.

PRIOR AND CURRENT PROGRESS

This past year was spent trying to complete the final experiment in a series of studies of sexual maturation in hyperthyroid female rats. We attempted to assess the positive feedback effect of estrogen on LH secretion, copying exactly a previous study. This failed. We were then forced to do a larger pilot study to verify the exact timing for this study in normal animals. This was completed, yielding some differences from the previous study, probably related to animal strain and environmental conditions. The estrogen-LH study has now been repeated in the hyperthyroid rats; results are pending at this time. Previous studies have characterized other aspects of growth and sexual maturation in hyperthyroid rats (see list of publications).

CONCLUSIONS

Hyperthyroidism accelerates growth but delays puberty in maturing female rats. The mechanism of the pubertal delay is not yet certain pending additional results.

REPORT DATE: 05/16/91

WORK UNIT # 1376-86

DETAIL SUMMARY SHEET

TITLE: Ketoconazole Effects on Vitamin D in Hypercalcemic Patients

KEYWORDS: ketoconazole, hypercalcemia, vitamin D

PRINCIPAL INVESTIGATOR: Glass, Allan COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Apr 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 18,811 Total: \$ 18,811

STUDY OBJECTIVE

To determine whether ketoconazole can reduce serum vitamin D levels and/or serum calcium levels in hypercalcemic patients, and to assess whether such reduction might be of diagnostic or therapeutic use.

TECHNICAL APPROACH

Measurement of serum calcium, PTH, and vitamin D metabolites in hypercalcemic patients before and after administration of ketoconazole 200 mg every 8 hours for 1 week.

PRIOR AND CURRENT PROGRESS

In prior years, this protocol was used to study normal subjects as well as patients with hyperparathyroidism and sarcoidosis. No additional patients were studied during the past fiscal year. Three papers and four abstracts have been published in previous years; no publications during FY91.

CONCLUSIONS

Ketoconazole reduces serum levels of 1,25-dihydroxyvitamin D in normal subjects and in patients with hyperparathyroidism or sarcoidosis.

REPORT DATE: 08/08/91

WORK UNIT # 1384-86

DETAIL SUMMARY SHEET

TITLE: Calcium Supplements and Calciuria in the Elderly

KEYWORDS: calcium, calciuria, elderly

PRINCIPAL INVESTIGATOR: Duncan, William MAJ MC

ASSOCIATES: Wray, H. Linton COL MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Sep 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 4,234 Total: \$ 4,234

STUDY OBJECTIVE

To determine if calcium carbonate given once a day (QD) or three times a day (TID) will cause hypercalciuria in elderly patients.

TECHNICAL APPROACH

Elderly patients will receive 900 mg of calcium carbonate (every a.m. or TID) or no supplement, in addition to a 660 mg standardized calcium diet. Urine and serum measurements will be done and analyzed.

PRIOR AND CURRENT PROGRESS

Fifteen patients have completed this protocol. Analyses of the data and chemical measurements have been done. Preliminary results of this study were presented at the 40th Annual Meeting of the Gerontological Society of America. The manuscript is being finalized for submission for publication. Since no further patient recruitment is anticipated, I request that this protocol be closed.

CONCLUSIONS

Calcium carbonate should be given in divided doses, and in elderly patients taking 1500 mg elemental calcium/d, the risk of hypercalciuria is small. In addition, parathyroid hormone (PTH) is suppressed with TID dosing rather than QD dosing.

REPORT DATE: 03/18/91

WORK UNIT # 1385-87

DETAIL SUMMARY SHEET

TITLE: Molecular Biology of Thyroid Disease

KEYWORDS: molecular, thyroid, biology

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Baker, James MAJ MC; Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Oct 1986

FUNDING: Current FY: \$ 1,748 Previous FYs: \$ 60,808 Total: \$ 62,556

STUDY OBJECTIVE

To clone the genes encoding for TSH receptor and TSH receptor antibody, and to characterize the receptor gene product.

TECHNICAL APPROACH

We have a cDNA for the TSH receptor. We will perform Southern blot analysis on lymphocytes and thyrocytes from patients with various types of thyroid disease, to include cancer, thyroiditis, and autoimmune disease. The Southern blot will be probed with several labelled inserts, to include immunoglobulin and T cell receptor probes, as well as viral probes; other growth factor probes, such as an epidermal growth factor receptor probe, can be used. We will also utilize oncogene probes and thyroglobulin probes to analyze expression in these tissues.

PRIOR AND CURRENT PROGRESS

We have been successful in isolating three proteins of approximately 18,000 and 65,000 molecular weight that are detected by our monoclonal antibody against the TSH receptor and not by controlled samples. We will further characterize these proteins as indicated in the system above. We have isolated these proteins by affinity chromatography utilizing TSH receptor antibody and will shortly sequence them.

CONCLUSIONS

The TSH receptor is composed of 18,000 and 65,000 molecular weight antigens. Intrathyroidal lymphocytes from patients with autoimmune disease show a polyclonal heterogeneity. C-myc expression is unchanged in thyroid cancer and autoimmune thyroid disease. EGF receptor gene may be rearranged in thyroid cancer.

REPORT DATE: 04/03/91

WORK UNIT # 1386-87

DETAIL SUMMARY SHEET

TITLE: In Vitro Determination of Messenger RNA Isolated from Porcine Thyroid Glands

KEYWORDS: messenger RNA, porcine, thyroid glands

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Baker, James MAJ MC; Peele, Mark CPT MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Dec 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 3,979 Total: \$ 3,979

STUDY OBJECTIVE

To utilize in vitro translation of thyroid messenger RNA in order to understand the array of thyroid specific proteins that are encoded and, further, to isolate and characterize important thyroid related proteins, such as the TSH receptor.

TECHNICAL APPROACH

Isolation of messenger RNA from pork thyroid glands is performed by standard GTC extraction techniques. The messenger RNA is obtained by poly A+ RNA chromatography, and the messenger RNA obtained is translated with an S labelled into specific proteins. These specific proteins are then electrophoresed on one or two dimensional gels, with the proteins obtained then identified. Both pork thyroid glands and hepatic samples are used. Also, specific antibodies can be utilized against the proteins to determine which proteins are of interest, such as to recognize the TSH receptor.

PRIOR AND CURRENT PROGRESS

We have performed approximately 10-15 translations and have identified specific proteins that are present in thyroid. We are in the process of identifying these proteins.

CONCLUSIONS

There are thyroid-specific proteins present within the thyroid glands that have various molecular weights. Specific efforts to identify the molecular weights of these proteins and their physical chemical determination are proceeding.

REPORT DATE: 05/09/91

WORK UNIT # 1387-87

DETAIL SUMMARY SHEET

TITLE: Dissolution of Commercial Oral Calcium Carbonate Supplements

KEYWORDS: dissolution, calcium

PRINCIPAL INVESTIGATOR: Duncan, William LTC MC

ASSOCIATES: Wray, H. Linton COL MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Jan 1987

FUNDING: Current FY: \$ 9,151 Previous FYs: \$ 29,853 Total: \$ 39,004

STUDY OBJECTIVE

To determine the in vitro dissolution of commercially available oral calcium carbonate supplements.

TECHNICAL APPROACH

Dissolution is being tested by method II of the U.S. Pharmacopeia.

PRIOR AND CURRENT PROGRESS

Twenty-seven calcium carbonate preparations have been tested, with only five meeting USP Standards. In vitro dissolution correlates with the filler content of each tablet but not with the stated calcium content, chemical sources of the calcium, retail cost, pill hardness, or retail source. A manuscript has been accepted for publication.

CONCLUSIONS

These results raise concern about the bioavailability of the calcium in these preparations.

REPORT DATE: 08/08/91

WORK UNIT # 1389-87

DETAIL SUMMARY SHEET

TITLE: 1,25-Dihydroxyvitamin D3 Induction of Ornithine Decarboxylase Activity
in Regenerating Rat Liver

KEYWORDS: 1,25-dihydroxyvitamin, ornithine decarboxylase, liver

PRINCIPAL INVESTIGATOR: Duncan, William LTC MC

ASSOCIATES: Wray, H. Linton COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: May 1987

FUNDING: Current FY: \$13,020 Previous FYs: \$ 0 Total: \$ 13,020

STUDY OBJECTIVE

To determine whether 1,25(OH)2D3 induces ornithine decarboxylase (ODC) activity via a receptor (genomic) mechanism in regenerating rat liver.

TECHNICAL APPROACH

ODC activity and oncogene expression are measured in regenerating liver from vitamin D deficient and vitamin D treated rats.

PRIOR AND CURRENT PROGRESS

We have shown that the hepatic nuclear 1,25(OH)2D3 receptor rapidly decreases in regenerating rat liver. Analysis of these changes with time demonstrates that the receptor decreases to 64% of basal concentrations 2 hours after hepatectomy and slowly returned to pre-hepatectomy values by 32 hours. ODC activity increases after hepatectomy to a maximum at 16 hours. We are currently analyzing changes in c-myc protooncogene mRNA expression by Northern Analysis. To date, these studies confirm our previous finding using dot blot analysis of a decrease in c-myc mRNA 2 hours after hepatectomy.

CONCLUSIONS

The rise in c-myc and ODC expression during liver regeneration is associated with a fall, not a rise, in expression of the vitamin D receptor. Thus, these activities may not be linked to receptor-mediated 1,25(OH)2D3 action in the regenerating liver.

REPORT DATE: 06/16/91

WORK UNIT # 1390-87

DETAIL SUMMARY SHEET

TITLE: Dynamic Assessment of Zinc Status in Thyroid Disease

KEYWORDS: zinc, hyperthyroidism, hypothyroidism

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Wartofsky, Leonard COL MC; Solomon, Barbara DNSc

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: May 1987

FUNDING: Current FY: \$44,476 Previous FYs: \$ 37,429 Total: \$ 81,905

STUDY OBJECTIVE

To understand zinc metabolism in thyroid disease.

TECHNICAL APPROACH

Measure zinc blood and urine levels in patients with thyroid disease. A zinc tolerance test is also given. A diet record is kept by the patient.

PRIOR AND CURRENT PROGRESS

Sixteen hypothyroid, five hyperthyroid, and eight normal volunteers have completed the study. All blood and urine samples have been analyzed, and the data is being computed. Our collaborators at USUHS have recently finished performing their aspects of the study, and we need to continue to meet with them for their analysis.

CONCLUSIONS

None.

REPORT DATE: 08/08/91

WORK UNIT # 1391-87

DETAIL SUMMARY SHEET

TITLE: Bone Mineral Density (BMD) in Patients with Chronic Renal Failure

KEYWORDS: bone mineral, renal failure

PRINCIPAL INVESTIGATOR: Duncan, William LTC MC

ASSOCIATES: Gouge, Steven MAJ MC; Moore, Jack LTC MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 814 Total: \$ 814

STUDY OBJECTIVE

To correlate bone mineral density measurements at the spine and forearm with clinical and laboratory parameters of patients with chronic renal failure.

TECHNICAL APPROACH

This is a pilot retrospective chart review of patients with chronic renal failure who have had forearm and spine bone mineral density measurements.

PRIOR AND CURRENT PROGRESS

Data collection is completed and analyzed. Results indicate that in chronic renal failure, bone loss is primarily cortical and that measurement of trabecular bone adds little to the evaluation of patients with chronic renal failure. A manuscript is in preparation.

CONCLUSIONS

Forearm densitometry is the test of choice to follow the status of bone in patients with chronic renal failure.

REPORT DATE: 08/23/91

WORK UNIT # 1393-87

DETAIL SUMMARY SHEET

TITLE: Regulation of Rat TSH Beta Subunit Gene Expression

KEYWORDS: TSH, gene, rodent

PRINCIPAL INVESTIGATOR: Carr, Frances PhD

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Aug 1987

FUNDING: Current FY: \$14,125 Previous FYs: \$ 128,378 Total: \$ 142,503

STUDY OBJECTIVE

To determine how the structure of the B-subunit gene of rat thyrotropin defines the functional response of the gene (including hormonal regulation) by thyroid hormones and tissue-specific expression.

TECHNICAL APPROACH

Chimaeric plasmids, encompassing various portions of the 5'-end of the rat TSH B-subunit gene, will be constructed by fusion of the eukaryotic gene sequence with the coding sequence of a reporter enzyme [specifically bacterial chloramphenicol acetyl transferase (CAT)]. Transient expression in eukaryotic cells will then be used to identify the cis elements responsible for hormonal regulation in a responsive cell line and those responsible for cell-specific expression in non-responsive cell lines. Then, DNA-protein interaction assay (DNase I protection and gel shift assays) will be used to identify DNA binding proteins that affect transcription, such as the thyroid hormone receptor.

PRIOR AND CURRENT PROGRESS

Thyroid hormone suppression of TSH gene expression occurs through the interaction of the thyroid hormone receptor binding to a sequence located in the first exon. The suppressive effects mediated by the CIS DNA elements occur when the sequences are fused to a non-thyroid hormone responsive gene (herpes simplex virus thymidine kinase promoter) both 5' and 3' to the transcriptional start site.

CONCLUSIONS

The negative thyroid hormone response element has been identified. The sequences are not the previously identified positive element. This negative element functions independently of promoter position. Therefore, thyroid hormone suppression of gene expression does not occur through steric hindrance, as postulated previously. This is a unique receptor-DNA action.

REPORT DATE: 08/12/91

WORK UNIT # 1394-87

DETAIL SUMMARY SHEET

TITLE: Molecular Biology of Nutrient Alterations in Rats

KEYWORDS: molecular biology, nutrition, glucose

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Carr, Frances PhD; Glass, Alan COL MC

DEPARTMENT: Department of Medicine

SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing

APPROVAL DATE: Aug 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 20,867 Total: \$ 20,867

STUDY OBJECTIVE

To examine changes in the insulin receptor and glucose transporter gene and T3 transcript in various states of nutrition.

TECHNICAL APPROACH

Rats are divided into eight dietary groups so that the effect of nutritional alterations can be studied in various aspects of DNA and RNA. There is a control, calorie restricted, high fat, pair fed, high sucrose and copper deficient group. After three months on the appropriate diet, the rats are sacrificed, and the organs are studied for transcription of various genes to include T3, transporter, insulin receptor, erb A, TSH receptor, and other oncogenes and proteins.

PRIOR AND CURRENT PROGRESS

Dr. Kushner had transferred to MAMC, which delayed progress on this project. Dr. Kushner is now back, and I expect progress to restart within 6-9 weeks.

CONCLUSIONS

None.

REPORT DATE: 09/13/91

WORK UNIT # 1395-87

DETAIL SUMMARY SHEET

TITLE: Oncogenes and Thyroid Receptors

KEYWORDS: oncogenes, thyroid

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Carr, Frances PhD; Baker, James MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$58,199 Previous FYs: \$ 86,470 Total: \$ 144,669

STUDY OBJECTIVE

To determine whether oncogenes are expressed variably in thyroid tissue derived from patients with different thyroid diseases. Further, patterns of DNA hybridization will help determine if amplified or rearranged genes exist.

TECHNICAL APPROACH

Nucleotides are subjected to gel electrophoresis and then transferred to nylon or nitrocellulose. These membranes are then probed with high specific activity P32 labelled inserts or plasmids. Results are quantitated visually and by spectrophotometer readings, after autoradiography and development. Abnormal patterns of hybridization may indicate expression abnormalities in RNA or amplification or rearrangement abnormalities in DNA.

PRIOR AND CURRENT PROGRESS

We have been very successful in developing and refining techniques to isolate, purify, electrophorese, transfer, and hybridize RNA and DNA. We have obtained samples from 30 patients with thyroid cancer, nodules, and goiter. Using c-Erb B gene probe, we have noted that several cell lines have rearranged genes, but none of the thyroid tissue analyzed shows a consistent abnormality. However, we have also examined c-myc patterns and again note no consistent abnormality. We plan to continue to study the thyroid cell lines that demonstrate gene rearrangements and also will now proceed to examine hybridization patterns to other oncogenes, such as Erb A, neu, her, myb, etc. Further, we will use other probes as they are developed, such as the TSH receptor probe or ANF probe, to help understand the abnormalities in thyroid tissue. Viral probes will also be used.

CONCLUSIONS

Thyroid cell lines may grow by virtue of the fact they have rearranged genes for growth factors, but other oncogenes, such as c-myc and c-Erb B probably do not play an integral role in determining how thyrocytes grow and divide.

REPORT DATE: 04/02/91

WORK UNIT # 1399-87

DETAIL SUMMARY SHEET

TITLE: Growth Factors and the Thyroid Gland

KEYWORDS: human thyroid, EGF, ANP

PRINCIPAL INVESTIGATOR: Tseng, Yueh-Chu PhD

ASSOCIATES: Wartofsky, Leonard COL MC; Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Dec 1987

FUNDING: Current FY: \$38,812 Previous FYs: \$ 51,686 Total: \$ 90,498

STUDY OBJECTIVE

To determine the role of epidermal growth factor (EGF), atrial natriuretic peptide (ANP) and their respective receptors in the maintenance of cultured human thyroid cells derived from surgically removed thyroids in various diseased states.

TECHNICAL APPROACH

1) Primary thyroid cell culture will be established by digesting human thyroid tissues with collagenase, collecting the thyroid cells, then growing cells in proper plates for experiments. 2) EGF and ANP receptors on thyroid cells will be assayed by Scatchard analysis to determine the number of receptor binding sites and their respective binding association constants. 3) Effects of EGF and ANP on thyroglobulin (Tg) secretion by thyroid cells will be determined by assaying Tg concentration media using ELISA. 4) ANP receptor will be characterized by affinity cross-linking using chemical reagent followed by electrophoresis gel separation.

PRIOR AND CURRENT PROGRESS

1) EGF receptor was found in medullary carcinoma cell line which was derived from C-cells located in thyroid gland. The addition of EGF to culture stimulated cell growth. 2) ANP internalization into thyroid cells was stimulated by the presence of TSH during binding assay. However, the overall ANP binding was inhibited by TSH. 3) ANP acts on thyroid cells through receptor to inhibit cyclic AMP and thyroglobulin production. The ANP receptor is a protein of 70 kD dalton.

CONCLUSIONS

Receptors for ANP, EGF, and TSH were found in cultured thyroid cells. Addition of ANP, EGF, or TSH, alone or in combination, to cells affect cyclic AMP and thyroglobulin production, receptor binding and internalization, as well as cell growth.

REPORT DATE: 11/25/91

WORK UNIT # 4299

DETAIL SUMMARY SHEET

TITLE: T-Cell Dysfunction as a Prognosticator for the Development of Autoimmune Thyroid Disease in Microsomal Antibody Positive Postpartum Women

KEYWORDS: thyroiditis, oncogenes, autoimmunity

PRINCIPAL INVESTIGATOR: Fein, Henry LTC MC

ASSOCIATES: Smallridge, Robert COL MC; Carr, Frances PhD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$13,443 Previous FYs: \$ 0 Total: \$ 13,443

STUDY OBJECTIVE

T-cell dysfunction may cause Autoimmune Thyroid Disease (AITD). Thyroid microsomal antigen stimulation may reveal alterations in postpartum microsomal antibody (MAB) positive patients, which may explain the causes of AITD and identify women who will develop clinical postpartum thyroid disease. T cells will be obtained from four groups of women: postpartum MAB positive (+) or negative (-), and non-postpartum MAB + or -.

TECHNICAL APPROACH

T-cells will be obtained at 0, 3, and 6 mos postpartum from MAB + or - subjects and once from non-postpartum subjects. IL-1 stimulation will look for nonspecific enhancement of immune function. Baseline and stimulatory measurements of c-fos, c-jun, and c-myc, IL-2 production, and cell proliferation via [3H] thymidine incorporation will be made. MAB levels will be analyzed in relation to specific incremental changes of the oncogenes, IL-2 production, and cell proliferation. Gestational alterations will be reflected by differences in our three test criteria when comparing postpartum versus non-pregnant MAB positives.

PRIOR AND CURRENT PROGRESS

Blood drawing: 20 patients will be enrolled in each group. FY91: Group I (PP,MAB+) - 8 subjects had T-cells obtained at 0, 3, 6 mos; 8 others are currently enrolled but not yet completed; 6 did not complete the protocol (blood obtained at 0 and 3 mos; subjects did not return at 6 mo. PP). Group II (PP,MAB-) - 4 subjects were completed; 10 enrolled but not yet completed; 6 did not complete. Group III (MAB+) - 7 subjects. Group IV (MAB-) - 20 subjects. T-cell function: All samples have undergone IL-1 stimulation; samples have been obtained for determinations of IL-2 production, cell proliferation. Cells have been processed to obtain oncogene mRNA levels.

CONCLUSIONS

Data are being actively accumulated at present. No definitive conclusions have been drawn yet.

REPORT DATE: 08/16/91

WORK UNIT # 4300

DETAIL SUMMARY SHEET

TITLE: Atrial Natriuretic Peptide and the Endometrium

KEYWORDS: ANP, endometrium, estrogen

PRINCIPAL INVESTIGATOR: Tseng, Yueh-Chu Ph.D.

ASSOCIATES: Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine
SERVICE: Endocrine-Metabolic Service

STATUS: Ongoing
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 9,013 Previous FYs: \$ 0 Total: \$ 9,013

STUDY OBJECTIVE

To analyze endometrial tissue preparations for the presence of ANP receptor and to demonstrate binding specificity; to culture endometrial cells in laboratory dishes and study ANP binding to viable cells; and to investigate the effects of sex steroids (estradiol and progesterone) on the development of ANP receptors.

TECHNICAL APPROACH

Frozen endometrium tissues will be homogenized in buffer, and membrane will be prepared by centrifugation. Membrane suspension will be incubated with [125I]-ANP at 4 C to determine specific binding to receptor. Freshly obtained endometrium will be digested in collagenase to isolate endometrial cells. Stromal cells will be isolated via differential trypsinization and cultured in 24-well plate at the density of 100,000 cells/well. ANP binding will be studied on cells pretreated with various concentrations of sex steroids.

PRIOR AND CURRENT PROGRESS

Tissue from 30 subjects has been studied. After incubation at 4 C for 3 hours, [125I]-ANP specifically bound to membrane preparation of endometrium. In cultured stromal cells, specific, high affinity ($K_d=0.17$ nmol/L) and low capacity (35,760 binding sites/cell) was observed. In cultured stromal cells, increasing concentrations of ANP dose-responsively stimulated cyclic-GMP production, a five-fold increase at 100 nmol/L ANP was observed. Addition of ANP to cells had no effect on cyclic ANP production.

CONCLUSIONS

A specific high affinity receptor for ANP was identified in human endometrial cells. ANP action on endometrium is probably mediated through cyclic GMP pathway.

REPORT DATE: 06/13/91

WORK UNIT # 4539

DETAIL SUMMARY SHEET

TITLE: Nasal Radioiodine Activity: A Study of Frequency, Intensity and Pattern

KEYWORDS: iodine, thyroid cancer

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Neutze, Janet MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if nasal radioiodine uptake is normal.

TECHNICAL APPROACH

Scans from people with thyroid cancer are reviewed by an unbiased observer in a single-blinded fashion. The amount of uptake in the nasal area is identified and quantitated. In this manner, we studied 221 patients scans and found that 15 of 20 were positive for uptake in the nasal area, but there was no evidence of activity elsewhere and the thyroglobulins were low. We concluded that the nasal activity did not represent authentic return of thyroid cancer.

PRIOR AND CURRENT PROGRESS

See above. Nasal activity is considered a normal uptake and should not be treated with radioiodine.

CONCLUSIONS

Radioiodine of the nasal activity is considered a normal variant that has not been recognized by Nuclear Medicine physicians.

REPORT DATE: 06/16/91

WORK UNIT # 9266

DETAIL SUMMARY SHEET

TITLE: The Treatment of Graves' Disease with Anti-Idiotypic Therapy Using Intravenous Immunoglobulin

KEYWORDS: Graves' disease, anti-idiotypic, IV immunoglobulin

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Baker, James MAJ MC; Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: May 1986

FUNDING: Current FY: \$ 2,275 Previous FYs: \$ 21,688 Total: \$ 23,963

STUDY OBJECTIVE

To determine if IV immunoglobulin alters thyroid function or antibody levels in patients with Graves' disease.

TECHNICAL APPROACH

Will infuse 4 grams per Kg daily for 3 days, and determine thyroid hormone levels and TBII and TSI levels before, during and after the infusion.

PRIOR AND CURRENT PROGRESS

We have performed these infusions on three people. Two of them did well, and the third did not feel well during the infusion. There were apparently no major alterations in the parameters measured. We plan to recruit a larger number of patients since there is very strong supportive evidence that these infusions might be helpful in this disorder.

CONCLUSIONS

None yet.

REPORT DATE: 08/15/91

WORK UNIT # 9273

DETAIL SUMMARY SHEET

TITLE: Identification and Characterization of Thyroid Autoantigens

KEYWORDS: thyroid, antigen, viral

PRINCIPAL INVESTIGATOR: Burman, Kenneth COL MC

ASSOCIATES: Humphrey, Michael CPT MC; Francis, Thomas CPT MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Endocrine-Metabolic Service

APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To identify viral-like particles in serum or thyroid tissue from patients with thyroid disease.

TECHNICAL APPROACH

Northern and Southern blots with viral probes, as well as PCR with viral and related particles, EB virus transformation, and hybridoma fusions for T and B cells are to be performed.

PRIOR AND CURRENT PROGRESS

Histone-related proteins and genes are uniquely found in thyroid tissue. We have preliminary data that HIV virus is not present in thyroid tissue, but we are continuing to pursue this area with a wide variety of viral probes. So far, three patients have been enrolled.

CONCLUSIONS

HIV is not related to the development of thyroid disease, but other, more unique viruses may be found.

REPORT DATE: 06/21/91

WORK UNIT # 1400-88

DETAIL SUMMARY SHEET

TITLE: A Pilot Study Evaluating Intestinal and Serum Immunoglobulin Levels in Patients with Acquired Hypogammaglobulinemia and Recurrent/Chronic Diarrhea of Undefined Etiology

KEYWORDS: immunoglobulin, hypogammaglobulinemia, diarrhea

PRINCIPAL INVESTIGATOR: Engler, Renata LTC MC

ASSOCIATES: Shea, Steve COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 2,658 Total: \$ 2,658

STUDY OBJECTIVE

a) To develop an IgG-subclass specific ELISA for measurement of G1/G2/G3 and G4 levels in intestinal secretions; b) To measure quantitative immunoglobulin levels, particularly IgG subclasses, in the intestinal secretions of patients with common variable hypogammaglobulinemia and compare these with normal levels.

TECHNICAL APPROACH

Secretions previously collected under protocol #1453 (normals) and those stored from medically indicated evaluations (hypogammaglobulinemic patients with diarrhea) will be utilized for study. An ELISA utilizing highly specific monoclonal antibodies to human G subclasses will be developed. Results are to be standardized to a uniform reference and quantitated in nanograms per mL.

PRIOR AND CURRENT PROGRESS

Initial baseline experiments were performed but were complicated by low level detection requirements and excessive background activity from secretions versus serum. Transfer of principal and collaborative investigators also hampered continued progress of the project. The IgG subclass assay has been refined and made more sensitive by employing a multi-antibody sandwich method.

CONCLUSIONS

Technical difficulties in the G subclass ELISA may be overcome by the availability of purified subclass reagents (previously only in ascites). This accomplishment, with recent improvement in technical support, should allow this work to progress.

REPORT DATE: 08/12/91

WORK UNIT # 1401

DETAIL SUMMARY SHEET

TITLE: The Effect of Normalization of Intraesophageal pH on Mucosal Proliferation in Barrett's Esophagus

KEYWORDS: Barrett's esophagus, gastroesophageal reflux, proliferation

PRINCIPAL INVESTIGATOR: Murphy, Joseph MAJ MC

ASSOCIATES: Maydonovitch, Corinne BS; Wong, Roy COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 4,014 Previous FYs: \$ 1,865 Total: \$ 5,879

STUDY OBJECTIVE

Barrett's esophagus (BE) is a columnar epithelium with premalignant potential which develops in response to prolonged and severe gastroesophageal reflux (GER). The study objective is to normalize the intraesophageal pH with omeprazole (Losec) and then observe the effect on mucosal proliferation as assessed by ornithine decarboxylase activity and thymidine uptake.

TECHNICAL APPROACH

Patients (10) with BE, who have reflux by 24 hour ambulatory esophageal pH study, will have esophagogastro-duodenoscopy (EGD) to obtain biopsies of BE to measure mucosal proliferation rate. Losec 20 mg po bid will be started; a pH study will be repeated after 1 week. If the esophageal pH is still <4, the dosage of Losec will be increased and the pH study repeated. When the esophageal pH >4 on repeat pH study, the Losec will be continued an additional 60 days. EGD with biopsies and pH study will be completed after 30 and 60 days on Losec. Five control patients (with gastric ulcers) will undergo three sequential EGD with at least 1 pH study to exclude GER.

PRIOR AND CURRENT PROGRESS

To date, 10 patients with Barrett's esophagus have been enrolled, with an additional 2 patients since May 1991. Nine of 10 patients have completed the study. In eight patients, the rectal mucosa has been studied for thymidine uptake. No control patients have been enrolled.

CONCLUSIONS

None at this time.

REPORT DATE: 04/11/91

WORK UNIT # 1403

DETAIL SUMMARY SHEET

TITLE: Ambulatory 24 Hour pH Monitoring: A Comparison of Antimony Vs. Glass pH Electrodes for Detecting Gastroesophageal Reflux (GER)

KEYWORDS: gastroesophageal reflux, 24 hr pH monitoring

PRINCIPAL INVESTIGATOR: Herrera, Jorge MAJ MC

ASSOCIATES: Wong, Roy COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Completed
APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 415 Total: \$ 415

STUDY OBJECTIVE

To compare the performance of antimony vs. glass pH electrodes in detecting episodes of gastroesophageal reflux (GER) during 24 hr pH monitoring of the esophagus.

TECHNICAL APPROACH

One glass and one antimony pH electrode will be simultaneously inserted into the esophagus of patients symptomatic of GER to a distance of 5cm above the lower esophageal sphincter, as determined on esophageal manometry. The electrodes will be connected to ambulatory recorders, and data will be recorded for 24 hrs. Six parameters of reflux and the overall score will be compared between the two pH systems to detect any significant differences.

PRIOR AND CURRENT PROGRESS

The technical difficulties of connecting the antimony electrode to the ambulatory monitor have been worked out via an interface. No subjects have been enrolled in this study. The principal investigator is no longer at WRAMC. This study is being closed.

CONCLUSIONS

No conclusions can be made.

REPORT DATE: 04/03/91

WORK UNIT # 1404

DETAIL SUMMARY SHEET

TITLE: Treatment of the Microscopic Colitis/Collagenous Colitis Syndrome with Sulfasalazine: A Double-Blind Crossover Controlled Trial

KEYWORDS: microscopic/collagenous, colitis, sulfasalazine

PRINCIPAL INVESTIGATOR: Pearce, William MAJ MC

ASSOCIATES: Moses, Frank LTC MC

DEPARTMENT: Department of Medicine

SERVICE: Gastroenterology Service

STATUS: Ongoing

APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 50 Previous FYs: \$ 50 Total: \$ 100

STUDY OBJECTIVE

To determine whether sulfasalazine is effective therapy for the microscopic colitis/collagenous colitis (mc/cc) syndrome.

TECHNICAL APPROACH

A retrospective review and a prospective, double-blind, placebo controlled crossover study of the efficacy of 12 weeks' treatment with oral sulfasalazine in patients with the mc/cc syndrome.

PRIOR AND CURRENT PROGRESS

Fourteen patients suspected to have the mc/cc syndrome have been reviewed to better define the population prior to the prospective trial. Patients with inflammation of the lamina propria (4/14) had greater clinical disease and stool weight. Sulfasalazine appeared to be effective in achieving a clinical response in selected patients. Four patients have been enrolled in the prospective arm of the study to date, but they did not fulfill histologic criteria for randomization to treatment.

CONCLUSIONS

The mc/cc syndrome causes chronic diarrhea. Histologic features correlate with clinical disease. Sulfasalazine appears to be effective in selected patients.

REPORT DATE: 06/14/91

WORK UNIT # 1406

DETAIL SUMMARY SHEET

TITLE: Campylobacter Pylori: Serologic Studies as a Measure of Efficacy of Treatment

KEYWORDS: helicobacter pylori, peptic ulcer, gastritis

PRINCIPAL INVESTIGATOR: Truesdale, Richard MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 3,142 Previous FYs: \$ 4,931 Total: \$ 8,073

STUDY OBJECTIVE

a) To determine if H. pylori is a chronic infection; b) To determine efficacy of treatment and whether antibody levels fall with successful eradication of H. pylori; and c) To determine if salivary antibodies are present in detectable amounts to predict infection with the organism.

TECHNICAL APPROACH

Patients known or suspected of harboring H. pylori undergo EGD with gastric biopsy to confirm the presence of the organism. A tube of blood is drawn and salivais collected for determination of antibody to the organism. If the organism is present, treatment with Pepto Bismol, tetracycline, and metronidazole is given for 3 weeks. Patients return 1 month and 6 months later for reevaluation.

PRIOR AND CURRENT PROGRESS

Sixty-five patients have been enrolled over the past two years. Forty-seven have completed the full protocol, while 12 are in the midst of the study.

CONCLUSIONS

H. pylori is a chronic infection persisting for >3 years in 22 out of 23 patients. Treatment efficacy is 80%. Antibodies fall with H. pylori treatment eradication. Saliva contains detectable amounts of antibody to H. pylori.

REPORT DATE: 06/12/91

WORK UNIT # 1407

DETAIL SUMMARY SHEET

TITLE: Effectiveness of Pneumatic Dilations in the Treatment of Achalasia

KEYWORDS: achalasia, pneumatic dilation

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) To study the efficacy of pneumatic dilations performed in patients at WRAMC. 2) To determine if manometric or esophageal emptying studies can predict success of dilation.

TECHNICAL APPROACH

Review charts of patients evaluated in the GI Clinic at WRAMC for achalasia. Data collection will include patient's symptoms and weight, esophageal manometry studies, and esophageal emptying studies prior to and 1 month after dilation.

PRIOR AND CURRENT PROGRESS

Data was obtained from the charts of 30 untreated achalasia patients, who were subsequently evaluated and treated at WRAMC over 6 years. Many patients underwent more than one dilation to give a total of 64 dilations. Over the past year charts have been reviewed for presenting symptoms and data recorded on the day of dilation. Some of the recorded data has been computerized for analysis and should be completed in the coming year.

CONCLUSIONS

Preliminary review of data showed that there were no perforations noted in the 64 dilations performed. Pneumatic dilation is a safe and effective treatment for achalasia.

REPORT DATE: 06 12 91

WORK UNIT # 1408

DETAIL SUMMARY SHEET

TITLE: Nocturnal Gastroesophageal Reflux--Factors Associated with Reflux
Events: A Retrospective Review of 24 Hour Esophageal pH Monitoring Data

KEYWORDS: nocturnal, gastroesophageal reflux, 24 hr pH monitoring

PRINCIPAL INVESTIGATOR: Mitchell, Douglas MAJ MC
ASSOCIATES: Maydonovitch, Corinne BS; Wong, Roy COL MC

DEPARTMENT: Department of Medicine STATUS: Ongoing
SERVICE: Gastroenterology Service APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To review 24 hr pH monitoring studies to identify behavioral and physiologic events associated with gastroesophageal reflux (GER) events.

TECHNICAL APPROACH

Review 24 hr pH studies performed in the WRAMC GI Clinic over the past 4 years to select two groups: 1) patients with significant GER, as defined by a monitoring score >20; and 2) a control group, patients evaluated for GER who had a score </-20. Reflux events in each group will be analyzed for time of day they occurred, relationship to meals, patient's posture, and duration of reflux episode.

PRIOR AND CURRENT PROGRESS

To date, chart review on 40 patients evaluated for GER during 1990 has been completed and is in the process of data entry into a computerized data base. Further chart reviews are needed, as well as computer data entry, prior to analysis.

CONCLUSIONS

No conclusions can be drawn at this time.

REPORT DATE: 08/06/91

WORK UNIT # 1409

DETAIL SUMMARY SHEET

TITLE: Comparison of Intravenous H2 Antagonists and Their Influence on Gastric Emptying in Humans

KEYWORDS: gastric emptying, H2 antagonists

PRINCIPAL INVESTIGATOR: Stamm, Carl MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 207 Previous FYs: \$ 1,100 Total: \$ 1,307

STUDY OBJECTIVE

To evaluate the effect of intravenous bolus administration of three H-2 antagonists (cimetidine, ranitidine and famotidine) on gastric emptying (GE) in humans.

TECHNICAL APPROACH

In a double blinded randomized manner, on four separate study days spaced at least 72 hours apart, subjects will undergo a standard gastric emptying test in Nuclear Medicine after receiving an intravenous bolus of placebo or an H-2 antagonist. Gastric emptying data will be collected for 150 min. Blood samples for drug levels will be drawn immediately after.

PRIOR AND CURRENT PROGRESS

Four gastric emptyings were performed on each of nine subjects after IV bolus injection of placebo or three histamine H2-receptor antagonists. Compared to placebo, H-2 antagonists affect the early phase, solid gastric emptying, but not late phase or overall emptying.

CONCLUSIONS

The finding that early phase gastric emptying is delayed by H-2 antagonists may be of clinical importance in patients with borderline emptying disorders. A manuscript is in process.

REPORT DATE: 04/08/91

WORK UNIT # 1410

DETAIL SUMMARY SHEET

TITLE: Open Label Trial of Low Dose Oral Pulse Methotrexate Therapy for
Primary Sclerosing Cholangitis

KEYWORDS: methotrexate, sclerosing, cholangitis

PRINCIPAL INVESTIGATOR: Moses, Frank LTC MC

ASSOCIATES: Larsen, Byran MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine possible efficacy of low-dose methotrexate in the treatment of primary sclerosing cholangitis.

TECHNICAL APPROACH

After baseline evaluation to rule out other potential etiologies of liver disease, the patient has an ERCP, liver biopsy, and HIDA scan. They are then placed on gradually increasing doses of methotrexate (up to a maximum dose of 25 mg weekly). The patients are followed on a monthly basis. At the end of 1 year, a total re-evaluation is performed, with treatment continued for an additional year.

PRIOR AND CURRENT PROGRESS

Total of six patients enrolled in study.

CONCLUSIONS

None yet.

REPORT DATE: 03/29/91

WORK UNIT # 1411

DETAIL SUMMARY SHEET

TITLE: The Effect of Lithium Carbonate on Gastric Emptying and
Gastrointestinal Hormones in Humans: A Double Blind Randomized Study

KEYWORDS: lithium, carbonate, gastric emptying

PRINCIPAL INVESTIGATOR: DeMarkles, Michael CPT MC

ASSOCIATES: Wong, Roy COL MC; Sjogren, Robert COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Gastroenterology Service

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 1,510 Previous FYs: \$ 0 Total: \$ 1,510

STUDY OBJECTIVE

To study the effect of lithium carbonate on gastric emptying and
gastrointestinal hormones in humans.

TECHNICAL APPROACH

Twenty patients will be given either placebo or lithium carbonate (300 mg PO
Q3hrs X 10 doses). A gastric emptying study with a concurrent
electrogastrogram will be done after each medication. Gastric hormone and
lithium levels will be drawn during the study.

PRIOR AND CURRENT PROGRESS

Thus far, one patient has completed the protocol. The study was officially
begun in March 1991.

CONCLUSIONS

None at this time.

REPORT DATE: 06/05/91

WORK UNIT # 1412

DETAIL SUMMARY SHEET

TITLE: Clinical and Serologic Evaluation of Blood Donors at Walter Reed Army Medical Center

KEYWORDS: hepatitis C antibody, blood donors

PRINCIPAL INVESTIGATOR: Phillips, Raymond MAJ MC

ASSOCIATES: Sjogren, Maria LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

(1) To survey blood donors for the prevalence of hepatitis C antibody, and (2) to determine the prevalence of chronic hepatitis in blood donors who are rejected for donation due to the presence of increased ALT/presence of hepatitis B core antibody.

TECHNICAL APPROACH

To determine the prevalence of hepatitis C antibody, blood donors (at the time of donation) will provide an additional sample of blood to be tested for the presence of hepatitis C antibody. The antibody studies will be performed in Dr. Sjogren's lab at WRAIR. To determine the significance of abnormal ALT or hepatitis B core antibody, blood donors with such an abnormality will be invited via mail to participate in the study.

PRIOR AND CURRENT PROGRESS

Ten of the initial 450 blood donors surveyed for the presence of hepatitis C (2.2%) were found to be positive. No further survey is planned. Ongoing enrollment of patients with elevated ALT or the presence of core antibody continues. Enrollment has been slow with only 11 patients registered so far.

CONCLUSIONS

1) The prevalence of hepatitis C in military personnel (2.2%) is slightly higher than in the general civilian population (1.0%). 2) No conclusions can be derived from the second half of the study at this time due to an insufficient number of patients.

REPORT DATE: 04/30/91

WORK UNIT # 1413

DETAIL SUMMARY SHEET

TITLE: Large Bowel Adenomatous Polyp Dietary Intervention Study-Clinical Centers

KEYWORDS: colon, fat, fiber

PRINCIPAL INVESTIGATOR: Kikendall, James LTC MC
ASSOCIATES: Wong, Roy COL MC; Mateski, Donna RD

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$34,319 Previous FYs: \$ 0 Total: \$ 34,319

STUDY OBJECTIVE

1) To determine whether a high fiber, low fat diet can reduce the recurrence of colonic adenomas; 2) To determine whether the diet modulates several putative intermediate markers of carcinogenesis (ODC activity, PCN antigen, labeling index); and 3) To determine the degree of correlation between recurrence of adenomas and modulation of markers.

TECHNICAL APPROACH

WRAMC is one of seven centers. Each center enrolls healthy subjects who have recently undergone colonoscopic removal of all adenomas. Subjects are randomized to no intervention or to a high fiber, low fat diet. Subjects randomized to diet are intensively counselled. Colonoscopy is repeated at 1 and 4 years, and all polyps are removed and examined histologically. Unprepped sigmoidoscopy is performed at entry 1, and 4 years to obtain mucosal samples for analysis for intermediate endpoints.

PRIOR AND CURRENT PROGRESS

We have been chosen as one of seven clinical centers. An interagency agreement has been signed providing a budget of more than \$2 million over 7 years. Donna Mateski, RD, has been hired as senior nutritionist/study coordinator. Study dietitians are now being recruited. Target date for beginning to recruit subjects is September 1991.

CONCLUSIONS

None - work in progress.

REPORT DATE: 05/07/91

WORK UNIT # 1414

DETAIL SUMMARY SHEET

TITLE: Case Control Study of Colonic Adenomas

KEYWORDS: colonic adenomas, risk factors, cartenoids

PRINCIPAL INVESTIGATOR: Kikendall, James LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$27,722 Previous FYs: \$ 0 Total: \$ 27,722

STUDY OBJECTIVE

To analyze previously collected data to define risk factors for colonic neoplasia.

TECHNICAL APPROACH

Three hundred and sixty-one subjects undergoing colonoscopy donated blood and urine samples and completed a dietary and environmental questionnaire from 1983-1987. Due to funding shortages, analysis of the collected data has been slow.

PRIOR AND CURRENT PROGRESS

Computer data entry was recently completed for polyp status, demographics, serum carotenoids, tocopherols, zinc, retinol, retinol binding protein, alcohol, tobacco, and all other collected data except the dietary questionnaire. Preliminary data analysis shows an inverse correlation of beta carotene and cryptoxanthin with adenomas and positive correlations of smoking and alcohol with adenomas. Although these factors are interrelated, they remain significant in multivariate analysis.

CONCLUSIONS

Pending further data analysis.

REPORT DATE: 05/15/91

WORK UNIT # 1415

DETAIL SUMMARY SHEET

TITLE: The Compassionate Use of Cisapride in the Treatment of Patients with Refractory Nonulcer Dyspepsia, Diabetic Gastroparesis with Intolerance to Metoclopramide and Chronic Intestinal Pseudoobstruction

KEYWORDS: cisapride, non-ulcer dyspepsia, diabetic gastroparesis

PRINCIPAL INVESTIGATOR: Shay, Steven COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To treat patients with refractory non-ulcer dyspepsia, diabetic gastroparesis, and intestinal pseudo-obstruction with Cisapride, a prokinetic agent not yet approved by the FDA.

TECHNICAL APPROACH

Patients are treated with 20 mg PO & id of Cisapride. Short-term treatment for 6 weeks is initiated. If symptomatic improvement occurs, the medication is continued long-term, as long as improvement continues. Appropriate blood tests and urinalysis are periodically obtained.

PRIOR AND CURRENT PROGRESS

One patient has completed short-term therapy, and has been in long-term therapy for 1 month.

CONCLUSIONS

The drug was effective in this one patient.

REPORT DATE: 05/27/91

WORK UNIT # 1416

DETAIL SUMMARY SHEET

TITLE: Association of Acromegaly and Intermediate Markers of Neoplasia

KEYWORDS: acromegaly, colonic neoplasia

PRINCIPAL INVESTIGATOR: Murphy, Joseph MAJ MC

ASSOCIATES: Schaaf, Marcus MD; Maydonovitch, Corinne BS

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 1,484 Previous FYs: \$ 0 Total: \$ 1,484

STUDY OBJECTIVE

To find the prevalence of colonic neoplasia in acromegalics, to identify risk factors, and to determine if there is a correlation between disease activity in acromegaly and intermediate markers of mucosal proliferation (ODC activity and tritiated thymidine uptake).

TECHNICAL APPROACH

Patients will have serum drawn for somatomedin C levels, undergo flexible sigmoidoscopy to obtain rectal tissue to measure ODC activity and tritiated thymidine uptake, and receive a colonoscopy to survey for colonic neoplasia.

PRIOR AND CURRENT PROGRESS

Thirty-one patients with acromegaly have been recruited and serum somatomedin C, flexible sigmoidoscopy, and colonoscopy performed. Colonoscopy results have been compared to 166 patients referred for heme + stools. No adverse reactions have been noted. Benefits to patients have included the diagnosis of adenomatous polyps in 12 patients. An additional two patients unexpectedly were diagnosed as having adenocarcinoma of the colon.

CONCLUSIONS

1) The prevalence of colonic neoplasia in patients over age 50 is 70% greater than patients with heme + stools. 2) Risk factors for colonic neoplasia are age and duration of disease. 3) Risk for adenocarcinoma is active disease greater than 10 years duration. 4) There is a significant correlation between ODC activity in colonic mucosa and serum somatomedin C.

REPORT DATE: 07/03/91

WORK UNIT # 1417

DETAIL SUMMARY SHEET

TITLE: Incidence of Gastric Mucosal Injury in Patients Ingesting Liquid Versus Solid Ibuprofen

KEYWORDS: Gastritis, mucosal injury, ibuprofen

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

ASSOCIATES: Maydonovitch, Corinne BS

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 3,602 Previous FYs: \$ 0 Total: \$ 3,602

STUDY OBJECTIVE

To determine if there is a difference in the incidence of gastric mucosal injury between liquid and solid forms of ibuprofen.

TECHNICAL APPROACH

To examine the gastric mucosa endoscopically before and after 3 days of a randomized course of either liquid or solid ibuprofen.

PRIOR AND CURRENT PROGRESS

To date, 23 patients have completed the study out of an anticipated total of 30. There have been no complications or adverse reactions to date.

CONCLUSIONS

None.

REPORT DATE: 04/04/91

WORK UNIT # 1435

DETAIL SUMMARY SHEET

TITLE: Genetic Linkage in Achalasia

KEYWORDS: achalasia, HLA typing, genetic linkage

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

ASSOCIATES: Maydonovitch, Corinne BS

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Completed
APPROVAL DATE: Dec 1980

FUNDING: Current FY: \$ 0 Previous FYs: \$ 239 Total: \$ 239

STUDY OBJECTIVE

To determine if there is a genetically related association in achalasia.

TECHNICAL APPROACH

Perform HLA typing on patients seen in the Gastroenterology Clinic with documented achalasia or other motor disorders of the esophagus.

PRIOR AND CURRENT PROGRESS

A total of 40 subjects (24 Caucasians, 16 Blacks) were studied under this protocol. No new subjects were studied this year. An addendum was submitted to collect data on a control group to strengthen the findings of the study. The DCI Review Committee voted to terminate this study, since it was active for 10 years, and suggested that a new protocol be written to study control subjects.

CONCLUSIONS

In this study, the Caucasian achalasia group had a positive association for the Class II HLA antigen, DQw1, and a negative correlation for the DRw53 antigen.

REPORT DATE: 08/30/91

WORK UNIT # 1450

DETAIL SUMMARY SHEET

TITLE: Adenomatous Colonic Polyps: A Vitamers and MFO Induction

KEYWORDS: colon polyps, vitamin A, beta-carotene

PRINCIPAL INVESTIGATOR: Kikendall, James LTC MC

ASSOCIATES: Burgess, Mary RD; Bowen, Phyllis RD PhD

DEPARTMENT: Department of Medicine

SERVICE: Gastroenterology Service

STATUS: Ongoing

APPROVAL DATE: Jul 1982

FUNDING: Current FY: \$ 0 Previous FYs: \$ 13,484 Total: \$ 13,484

STUDY OBJECTIVE

a) Case control portion: To evaluate risk factors for colonic adenomas. b) Intervention portion: To evaluate beta-carotene, 15mg po daily, as a colon cancer chemopreventive agent.

TECHNICAL APPROACH

a) Case control portion: Subjects who report for indicated colonoscopy who meet entry criteria are assessed by dietary and historical interview and sampling of blood and urine. Subjects with polyps (adenomas) and colonoscopy-negative controls are compared. b) Intervention Study: Subjects are randomized to receive placebo or beta-carotene after removal of colonic adenomas. Repeat colonoscopy assesses recurrence over the subsequent 3 years. Although beta-carotene is not known to have any harmful side effects, several potential side effects are monitored.

PRIOR AND CURRENT PROGRESS

The intervention was completed in 1990. No serious side effects due to beta carotene were observed in the 260 patients seen. Beta carotene 15mg gd was determined to be of no benefit in preventing the recurrence of colonic adenomas. The results will be presented at the October 1991 meeting of the American College of Gastroenterology. A manuscript is in preparation. We are also attempting to complete computer data entry for other factors (e.g., smoking, age, alcohol consumption, number of polyps prior to polyp recurrence). This is anticipated to be a slow process without funding for personnel to accomplish the task.

CONCLUSIONS

Beta carotene 15mg gd does not reduce the recurrence of colonic adenomas.

REPORT DATE: 04/04/91

WORK UNIT # 1453

DETAIL SUMMARY SHEET

TITLE: The Effect of Sodium Deprivation on Small Intestinal Water and
Electrolyte Transport

KEYWORDS: intestinal transport, sodium depletion

PRINCIPAL INVESTIGATOR: Decker, Robert MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Completed
APPROVAL DATE: Oct 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 49 Total: \$ 49

STUDY OBJECTIVE

To resolve the following questions: 1) What are the water and electrolyte transport rates in jejunum and ileum as determined by triple lumen perfusion in normal volunteers at WRAMC? and 2) What effect does salt restriction have on intestinal absorptive ability, determined by triple lumen tube intestinal perfusion?

TECHNICAL APPROACH

Volunteers are initially studied over a 2-day period as inpatients, during which time a triple-lumen tube is passed orally into the small intestine and positioned by fluoroscopy. Subsequently, a standard Ringer's-like solution, a glucose-sodium chloride solution, and a mannitol-sodium chloride solution are infused for a period of approximately 4 hours during each of the 2 days.

PRIOR AND CURRENT PROGRESS

A total of 19 subjects were studied under this protocol. No new patients were enrolled this year. The study is completed, and a manuscript is in progress.

CONCLUSIONS

Short-term sodium depletion has no appreciable effect on sodium or water transport in the ileum. Intestinal IgA secretion is significantly greater in the jejunum than in the ileum and does not correlate with water transport.

REPORT DATE: 08/15/91

WORK UNIT # 1462

DETAIL SUMMARY SHEET

TITLE: The Evaluation of Postprandial Supine Reflux Events by Simultaneous Esophageal Manometry, Esophageal pH Monitoring, and Gastroesophageal Scintiscanning in Patients with Hiatus Hernia and Esophagitis

KEYWORDS: reflux, manometry, scintigraphy

PRINCIPAL INVESTIGATOR: Shay, Steven COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1983

FUNDING: Current FY: \$ 220 Previous FYs: \$ 2,921 Total: \$ 3,141

STUDY OBJECTIVE

To correlate the presence, approximate volume, and clearance of gastroesophageal reflux by scintiscan with reflux events and clearance as determined by pH changes. To evaluate temporal relationships of hiatal hernia filling and emptying as determined by scintiscan, with gastroesophageal reflux determined by scintiscan and pH changes.

TECHNICAL APPROACH

Patients with symptoms of gastroesophageal reflux and severe endoscopic esophagitis are included. An esophageal pH probe and manometer catheter are passed per nares to measure simultaneous manometry and pH monitoring. The patients ingest a study meal consisting of commercial beef stew, 15 lamb liver cubes, and 250 cc of water, each labeled with 50 uCu of 99m Technesium sulfur-colloid. The patients lie on the left and right side alternately for a total of 4-10 minute recumbent monitoring periods.

PRIOR AND CURRENT PROGRESS

We have studied a total of four patients to date; none since last year. This was to some extent due to a moratorium on research studies in nuclear medicine. Also, patients with large hiatal hernias and a good LES pressure and esophagitis are hard to find. There has been no incidence of serious or unexpected adverse reactions. A manuscript has been published dealing with other aspects of the study.

CONCLUSIONS

Scintigraphy discerns postprandial reflux episodes and their clearance better than the pH probe. The role of hiatal hernia is pending.

REPORT DATE: 08/06/91

WORK UNIT # 1470

DETAIL SUMMARY SHEET

TITLE: Intestinal Sodium and Water Transport: Evaluating Solutions to Maximize Absorption

KEYWORDS: short bowel syndrome, intestinal absorption, intestinal transport

PRINCIPAL INVESTIGATOR: Decker, Robert MAJ MC

ASSOCIATES: Wong, Roy COL MC

DEPARTMENT: Department of Medicine

SERVICE: Gastroenterology Service

STATUS: Completed

APPROVAL DATE: Aug 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,567 Total: \$ 1,567

STUDY OBJECTIVE

To evaluate oral rehydration formulas (ORF's) containing different carbohydrate moieties to determine an optimal solution for treatment of short bowel syndrome and acute diarrheal illnesses.

TECHNICAL APPROACH

The first part of the study utilizes the triple-lumen intestinal perfusion technique in normal volunteers to assess the relative contribution of active versus passive carbohydrate absorption in promoting salt and water absorption. In the second part, ORF's are infused in patients with short bowel syndrome, with measurements of ostomy output used to assess efficacy. There have been two minor protocol modifications. The first relates to solution infusion rate -- in part B this has been increased to 150ml/hr from 100ml/hr. The second modification deleted codeine IM and substitutes paregoric 10 cc orally as the antiperistaltic agent.

PRIOR AND CURRENT PROGRESS

Four patients have been studied under this protocol. No new patients were accessioned into the study this fiscal year as the Principle Investigator is no longer at WRAMC. There has been no incidence of serious or unexpected adverse reactions.

CONCLUSIONS

The data suggests that the World Health Organization oral rehydration formula is more efficient than a Polycose-electrolyte solution.

REPORT DATE: 08/06/91

WORK UNIT # 1471

DETAIL SUMMARY SHEET

TITLE: Serum and Tissue Zinc Levels in the Esophagus

KEYWORDS: zinc, esophagus

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

ASSOCIATES: Maydonovitch, Corinne BS

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Gastroenterology Service

APPROVAL DATE: Aug 1984

FUNDING: Current FY: \$ 160 Previous FYs: \$ 1,549 Total: \$ 1,709

STUDY OBJECTIVE

To determine zinc levels in serum, gastric fluid, and esophageal tissue of patients with upper gastrointestinal diseases, such as squamous cell carcinoma, reflux esophagitis, duodenal and gastric ulcer disease, and in normals.

TECHNICAL APPROACH

At the time of endoscopy, 15 cc of blood and biopsy tissue samples will be obtained and frozen in zinc-free tubes. Tissue samples will be dissolved in HCL and then analyzed for zinc. Blood and gastric fluid will also be analyzed after centrifugation by atomic absorption spectrophotometry.

PRIOR AND CURRENT PROGRESS

Serum, gastric fluid, and biopsy tissue of 113 patients with endoscopic findings (including esophagitis, gastritis, duodenal ulcer, or normal) have been analyzed under this study. There has been no incidence of serious or unexpected adverse reactions. In the past year emphasis was placed on revising a manuscript for publication.

CONCLUSIONS

The data shows that with esophagitis, zinc concentrations significantly increase in esophageal tissue and significantly decrease in serum.

REPORT DATE: 06/12/91

WORK UNIT # 1483

DETAIL SUMMARY SHEET

TITLE: Evaluation of Gastroesophageal Reflux as a Cause of Hoarseness

KEYWORDS: hoarseness, reflux, esophagitis

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

ASSOCIATES: Murphy, Joseph MAJ MC; Maydonovitch, Corinne BS

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Gastroenterology Service

APPROVAL DATE: Apr 1986

FUNDING: Current FY: \$ 11 Previous FYs: \$ 2,329 Total: \$ 2,340

STUDY OBJECTIVE

To determine if gastroesophageal reflux (GER) is a cause of "idiopathic" hoarseness.

TECHNICAL APPROACH

Patients with idiopathic hoarseness and characteristic ENT findings undergo standard GI evaluation for GER. If GER is identified, the patient undergoes baseline voice harmonic analysis and is reevaluated after 8 weeks of medical therapy.

PRIOR AND CURRENT PROGRESS

A total of 17 patients who had idiopathic hoarseness were screened for gastroesophageal reflux (GER). No new patients were accessioned this past year. There have been no withdrawals for adverse effects from this study.

CONCLUSIONS

Although more patients need to be studied, the data thus far indicates that gastroesophageal reflux is a common occurrence in patients with idiopathic hoarseness.

REPORT DATE: 08/06/91

WORK UNIT # 1487

DETAIL SUMMARY SHEET

TITLE: Prospective Evaluation of the Effect of Medical Therapy on Plasma and Tissue Zinc Levels in Esophagitis

KEYWORDS: zinc, esophagitis, GERD

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Jul 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,158 Total: \$ 1,158

STUDY OBJECTIVE

To prospectively evaluate the effect of anti-gastroesophageal reflux therapy on plasma and esophageal tissue zinc concentrations; and to determine if a correlation exists between degree of esophageal inflammation and plasma and esophageal zinc concentration.

TECHNICAL APPROACH

Patients with endoscopically proven peptic esophagitis undergo esophageal biopsy and phlebotomy for tissue and serum zinc concentration. After standard medical anti-reflux therapy, tissue and blood specimens are obtained for comparison zinc concentrations.

PRIOR AND CURRENT PROGRESS

Twelve patients have been studied before and after anti-gastroesophageal reflux therapy. Technical difficulties were met in analyzing zinc concentrations in the plasma and tissue samples collected. Over the past year, no new patients were accessioned into the study. However, the DCI General Support Lab has been active in developing a mechanism by which samples can be successfully analyzed.

CONCLUSIONS

No conclusions can be drawn at this time.

REPORT DATE: 04/01/91

WORK UNIT # 1489

DETAIL SUMMARY SHEET

TITLE: The Evaluation of Post prandial Supine Reflux Events by Simultaneous Esophageal Manometry, Esophageal pH Monitoring and Gastroesophageal Scintiscanning in Patients with Progressive Systemic Sclerosis with Severe Endoscopic Esophagitis

KEYWORDS: manometry, pH monitoring, scintigraphy

PRINCIPAL INVESTIGATOR: Murphy, Joseph MAJ MC

ASSOCIATES: Peller, Patrick MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Dec 1986

FUNDING: Current FY: \$ 878 Previous FYs: \$ 450 Total: \$ 1,328

STUDY OBJECTIVE

To determine whether the predominant pathophysiologic abnormality responsible for excessive esophageal exposure in patients with progressive systemic sclerosis (PSS) and severe endoscopic esophagitis is frequent reflux events, poor clearance of a few reflux events, or both.

TECHNICAL APPROACH

Patients with (1) endoscopic reflux esophagitis and abnormal 24 hour pH monitoring, and (2) scleroderma from the study population were included. Simultaneous manometry (esophageal motor activity), scintigraphy (reflux volume), and pH monitoring are performed for 40 minutes after a test meal labelled with 1.0 m Cu 99m Tc sulfur colloid.

PRIOR AND CURRENT PROGRESS

Three additional patients have been studied in the past year, which brings the total to eight.

CONCLUSIONS

The results of the study have shown that decreased smooth-muscle peristalsis appears to be the primary contributor to acid exposure and esophageal injury.

REPORT DATE: 06/05/91

WORK UNIT # 1493

DETAIL SUMMARY SHEET

TITLE: A Study to Evaluate the Development of Quantitative Analysis of
Video-digital Images Obtained During Esophagogastroduodenoscopy

KEYWORDS: videoendoscopy

PRINCIPAL INVESTIGATOR: Moses, Frank LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Completed
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 390 Total: \$ 390

STUDY OBJECTIVE

a) To develop an image collecting procedure that will permit quantitative image analysis; b) To develop disease oriented quantitative image analysis; and c) To evaluate the utility of quantitative image analysis in endoscopic diagnosis of GI disease.

TECHNICAL APPROACH

This is a multicenter protocol. This institution, along with others, has the primary task of obtaining endoscopic photographs taken with video-digital technology of esophageal erosions and duodenal ulcers. These photographs are stored in computer format and sent to a separate center for further analysis of size, shape, and other topographic characteristics.

PRIOR AND CURRENT PROGRESS

No further work has been performed on this protocol during the past fiscal year. Since FY89, the multicenter organizers have been postponing further work on this protocol pending redevelopment of photographic and computer hardware used in the system. Because of the low probability of any future progress, this protocol is closed.

CONCLUSIONS

The protocol is closed. No conclusions are available.

REPORT DATE: 03/06/91

WORK UNIT # 1495

DETAIL SUMMARY SHEET

TITLE: Effect of Beta-Carotene on Mucosal Proliferation : Patients with
Colonic Carcinoma

KEYWORDS: beta-carotene, colon carcinoma, proliferation

PRINCIPAL INVESTIGATOR: Phillips, Raymond MAJ MC

ASSOCIATES: Wong, Roy COL MC, Kikendall, James LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 1,185 Previous FYs: \$ 2,975 Total: \$ 4,160

STUDY OBJECTIVE

To determine the effect of beta-carotene on colonic epithelial proliferation in patients with resected adenocarcinoma of the colon or rectum.

TECHNICAL APPROACH

Patients with previously resected colon carcinoma are studied prior to and at 2, 9, 16, 24, and 28 weeks after receiving beta-carotene, 30mg PO QD. At each time point, biopsies and blood samples are obtained. Rectal mucosal biopsies are assayed for cell proliferation by tritiated thymidine uptake and ODC levels. Blood samples are analyzed for beta-carotene levels.

PRIOR AND CURRENT PROGRESS

Twenty patients have been enrolled and completed the study. Tissue obtained during the study is now being evaluated to assess proliferation rate; specifically, the proliferative rate at the different time points. This is a laborious stage and requires the daily attention of a trained technician. A technician is being trained at this time. There have been no adverse effects of the use of beta carotene.

CONCLUSIONS

With the initiation of beta-carotene there was a decrease in proliferation, as measured by ornithine decarboxylase (ODC) activity. This normalization of proliferation was significantly diminished at 2 and 9 weeks. During 16 and 24 weeks of therapy the rate was diminished, but not significantly. With discontinuation of therapy, ODC activity returned toward baseline. This study has implications for the prevention of colon cancer.

REPORT DATE: 04/04/91

WORK UNIT # 1496

DETAIL SUMMARY SHEET

TITLE: The Effects of Non-Steroidal Anti-Inflammatory Drugs on the Secretion of Human Salivary Epidermal Growth Factor

KEYWORDS: epidermal growth factor, saliva, anti-inflammatory drugs

PRINCIPAL INVESTIGATOR: Wong, Roy COL MC

ASSOCIATES: Maydonovitch, Corinne BS; Dutta, Sudhi MD

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 525 Total: \$ 525

STUDY OBJECTIVE

To determine if therapeutic doses of non-steroidal anti-inflammatory drugs affect salivary epidermal growth factor (EGF) secretion in humans.

TECHNICAL APPROACH

In a double-blind, randomized manner, volunteer subjects receive, on separate occasions two weeks apart, placebo TID for 3 days or indomethacin, 50 mg TID for 3 days. On the following morning, after a final drug dose, saliva is collected in a centrifuge tube, centrifuged, stored at -70C and analyzed by radioimmunoassay for EGF. Serum samples are collected and analyzed for indomethacin levels.

PRIOR AND CURRENT PROGRESS

A total of 21 volunteer subjects were studied. No new subjects were enrolled this year. One patient received placebo twice and was dropped from the data analysis. Data has been collated, and a manuscript is in progress.

CONCLUSIONS

Indomethacin significantly decreases salivary epidermal growth factor. This may play a role in the ulcerogenic properties of indomethacin.

REPORT DATE: 04/02/91

WORK UNIT # 1497

DETAIL SUMMARY SHEET

TITLE: The Effect of Indomethacin on Rectosigmoid Mucosal Blood Flow and Rectosigmoid Mucosal Prostaglandin Levels in Humans

KEYWORDS: indomethacin, rectosigmoid, laser Doppler

PRINCIPAL INVESTIGATOR: Murphy, Joseph MAJ MC

ASSOCIATES: Wong, Roy COL MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,250 Total: \$ 1,250

STUDY OBJECTIVE

To determine the effect of prostaglandin synthesis inhibition on rectosigmoid mucosal blood flow and rectosigmoid mucosal prostaglandin E2 levels.

TECHNICAL APPROACH

In a double-blind, randomized fashion, each subject will receive, on two separate occasions separated by 2 weeks, either placebo TID for 3 days or indomethacin, 50mg TID for 3 days. The morning after the final dose of placebo or indomethacin, rectosigmoid mucosal blood flow will be measured with a laser-Doppler probe inserted through the biopsy channel of an endoscope. Two rectal mucosal biopsies will also be obtained to measure tissue prostaglandin levels and blood samples will be taken to measure indomethacin levels.

PRIOR AND CURRENT PROGRESS

No new subjects were added during the previous year. The fiber optic probes have been found to be sensitive to incandescent lights, requiring the installation of an opaque jacket.

CONCLUSIONS

Awaiting adjustments of optic probe to continue study.

REPORT DATE: 03/20/91

WORK UNIT # 1498

DETAIL SUMMARY SHEET

TITLE: Pathophysiology and Treatment for Non-Ulcer Dyspepsia (Using Cisapride)

KEYWORDS: non-ulcer dyspepsia, irritable bowel syndrome, Cisapride

PRINCIPAL INVESTIGATOR: Shay, Steven COL MC

ASSOCIATES: Maydonovitch, Corinne BS

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Dec 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare gastric motility and electrophysiology in patients with non-ulcer dyspepsia vs. normal volunteers. To determine the effect of a prokinetic agent, Cisapride, on symptoms and objective tests in patients with non-ulcer dyspepsia in a double-blind, crossover placebo controlled fashion.

TECHNICAL APPROACH

Patients with dyspeptic symptoms, in whom ulcer has been rigorously excluded, are studied. Three hour electrogastrograms and 24 hour antral motility evaluations are performed after treatment with placebo and cisapride. Changes in symptoms are measured using a questionnaire. A double-blind crossover design is employed so that each subject receives both placebo and cisapride.

PRIOR AND CURRENT PROGRESS

A total of five patients have been enrolled and completed the protocol. Initial data regarding gastric motility is being digitized.

CONCLUSIONS

None at this time. Study is a double-blinded, placebo controlled study, and more patients have to be enrolled.

REPORT DATE: 08/26/91

WORK UNIT # 2031

DETAIL SUMMARY SHEET

TITLE: Gastrointestinal Blood Loss During Marathon Running and the Effect of Cimetidine on its Prevention

KEYWORDS: GI blood loss, marathon running, cimetidine

PRINCIPAL INVESTIGATOR: Moses, Frank LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Gastroenterology Service

STATUS: Ongoing
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 602 Total: \$ 602

STUDY OBJECTIVE

To determine the frequency and severity of gastrointestinal blood loss during marathon and endurance exercise, and the effects of cimetidine on its prevention.

TECHNICAL APPROACH

Qualitative and quantitative stool hemoglobin analyses are performed before and after runners complete endurance competitive events.

PRIOR AND CURRENT PROGRESS

Two 100 mile ultramarathon events have been completed, and results have been analyzed. GI bleeding occurred in the majority of competitors, and GI symptoms were severe at times. It appears from an unblinded portion of the study that cimetidine offered protection to runners. Thirty of planned 250 marathon runners have been studied and, while results show a trend toward improvement with cimetidine, interpretation of prospective blinded data is limited by small numbers. A modification of the protocol has been submitted to allow endoscopy of some participants in order to localize bleeding.

CONCLUSIONS

Data suggests cimetidine may be of benefit in improving GI symptoms associated with endurance running and reduction of GI bleeding. Further evaluation and study of this condition is warranted and planned.

REPORT DATE: 11/19/91

WORK UNIT # 1024

DETAIL SUMMARY SHEET

TITLE: Candida Urinary Tract Infections: A Retrospective Review of Candida UTI's in Patients Hospitalized in a Tertiary Care Facility

KEYWORDS: Candida, urinary tract, infection

PRINCIPAL INVESTIGATOR: Mitchell, Douglas MD

ASSOCIATES: Hicks, Charles, LTC MC

DEPARTMENT: Department of Medicine
SERVICE: General Medicine Service

STATUS: Completed
APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To observe retrospectively Candida urinary tract infections study, looking for predisposing factors, treatments employed, and effect of treatment on outcomes.

TECHNICAL APPROACH

Retrospective chart review.

PRIOR AND CURRENT PROGRESS

This protocol is being closed at this time. The Principal Investigator has been transferred to a Public Health Service assignment. He hopes to continue this work when he returns to WRAMC in 2-3 years.

CONCLUSIONS

None.

REPORT DATE: 04/16/91

WORK UNIT # 1025

DETAIL SUMMARY SHEET

TITLE: Affective Features of Patients' Illness Descriptions: An Unappreciated Source of Variability in Physicians' Practice Patterns

KEYWORDS: variation, interviewing

PRINCIPAL INVESTIGATOR: Birdwell, Brian MAJ MC

ASSOCIATES: Kroenke, Kurt LTC MC; Herbers, Jerome MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: General Medicine Service

STATUS: Completed
APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

(1) To ascertain the degree and sources of variability in physician's initial assessment of patients' symptomatology; (2) To measure how initial impressions are altered by additional objective data; and (3) To contrast the effect of patient case presentation in different media (written vs. video format).

TECHNICAL APPROACH

A case vignette of a simulated patient encounter, using the exact same words, was prepared in three formats: (1) Videotape 1 (VT1) -- patient with chest pain describing her symptoms in histrionic fashion; (2) Videotape 2 (VT2) -- patient describing symptoms in businesslike fashion; and (3) Written transcript (WT) of same vignette. Physicians were randomized to see/read one of the three formats and then fill out a questionnaire on diagnostic impressions and plan of action.

PRIOR AND CURRENT PROGRESS

Forty-four physicians were randomized to see each of the three formats. There were no adverse reactions or withdrawals.

CONCLUSIONS

Physicians who saw the histrionic presentation (VT1) had twice the likelihood of listing a functional (as opposed to a cardiac) diagnosis for the patient's symptoms and were much less likely to do further testing. We conclude that a patient's style of reporting symptoms can override objective data regarding diagnostic impressions and further workup.

REPORT DATE: 04/16/91

WORK UNIT # 1026

DETAIL SUMMARY SHEET

TITLE: Dizziness: A Prospective Study of Patient Characteristics and Outcome

KEYWORDS: dizziness, etiology, prognosis

PRINCIPAL INVESTIGATOR: Kroenke, Kurt LTC MC

ASSOCIATES: Wehrle, Allen LTC MC; Rosenberg, Michael LTC MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: General Medicine Service

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To prospectively evaluate patients with a chief complaint of dizziness in order to determine the most common causes, the psychiatric and functional characteristics, the value of physical and laboratory examination, and the outcome at 4 and 12 months of follow-up.

TECHNICAL APPROACH

Patients seen for dizziness in four clinical areas (Internal Medicine Clinic, Outpatient Clinic, Neurology Clinic, and Emergency Room) are entered in a log book and contacted by phone to determine their willingness to participate. Participants were seen in the Dizziness Clinic where they underwent medical and psychiatric interviews, laboratory testing, audiologic testing, neuro-ophthalmologic examination, and detailed determination of their functional status. Follow-up (by mail) was performed at 4 and 12 months to determine outcome. Controls from the same clinical areas were recruited and underwent identical evaluation.

PRIOR AND CURRENT PROGRESS

A weekly Dizziness Clinic was held on Thursdays from May 1990 to April 1991, and we have completed study of 100 dizzy patients and 25 controls. There have been no adverse reactions or patient withdrawals. Pertinent findings from the study were forwarded, when appropriate, to the subject's primary health care provider. During the coming 12 months, we will be completing the follow-up phase of the study and will be analyzing the data.

CONCLUSIONS

Data analysis is just beginning, and we should have findings to report by this summer.

REPORT DATE: 08/27/91

WORK UNIT # 1507

DETAIL SUMMARY SHEET

TITLE: WRAMC 9010: A NCI-WRAMC Collaborative Phase I Study of Tetraplatin

KEYWORDS: Phase I, Tetraplatin, pharmacokinetics

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Hematology-Oncology Service

APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To establish the maximum tolerated dose, to carefully assess toxicities, to measure pharmacokinetics and DNA adduct formation, and to assess antitumor activity using Tetraplatin.

TECHNICAL APPROACH

Cohorts of three patients will be evaluated at each dose level until the maximum tolerated dose is reached. Initial dose of 4.3mg/m², with escalation according to Fibonacci scheme, will be given; we are now dosing at the 8th dose level. Close monitoring for toxicities will be maintained. Treatment will continue in each patient until progression of disease or six cycles have been given.

PRIOR AND CURRENT PROGRESS

There have been six patients registered from WRAMC. One patient remains on treatment, and it is too early to evaluate his response. The other five patients have been taken off treatment due to progressive disease. The maximum tolerated dose has not been reached. Toxicities have been minor. The most significant have been nausea and vomiting, which we are able to control with antiemetics.

CONCLUSIONS

The study is ongoing and has not reached its objectives at this time.

REPORT DATE: 08/14/90

WORK UNIT # 1616-82

DETAIL SUMMARY SHEET

TITLE: Phenotypic Characterization of Granulocytic Leukemia Blast Cells by High Performance Liquid Chromatographic Analysis of Cellular Proteins

KEYWORDS: CML, protein analysis, HPLC + electrophoresis

PRINCIPAL INVESTIGATOR: Bednarek, Jana MD

ASSOCIATES: Knight, Robert LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Completed
APPROVAL DATE: Sep 1982

FUNDING: Current FY: \$ 0 Previous FYs: \$ 2,144 Total: \$ 2,144

STUDY OBJECTIVE

Do granulocytes, mature and immature, circulating in blood or obtained from bone marrow, contain any phenotypic marker proteins as determined by HPLC and electrophoresis (and possibly immunochemical methods) that might serve as clinical indicators for: a) classifying CML patients into prognostic and therapeutic categories, b) predicting the onset of blast crisis, and/or c) early diagnosis?

TECHNICAL APPROACH

Mature and immature granulocytes obtained from normal volunteer blood or bone marrow, or peripheral blood from CML patients in different stages of their disease, were prepared with purity better than 90%, as described previously. In select preparations, we also prepared subcellular fractions. Proteins were extracted, as described previously, and separated by reverse phase HPLC and SDS slab gel electrophoresis of HPLC fractions. A pattern of select proteins was followed with the progression of the disease.

PRIOR AND CURRENT PROGRESS

We developed a method which allows us to study qualitatively and semi-quantitatively a large number of proteins contained in different parts of the cell. Granulocytes were studied from peripheral blood of 31 CML patients, 25 healthy volunteers, and 9 with bone marrow diseases that served as controls. CML patients were followed over a period of time, in conjunction with returning for treatments. A pattern emerged of selected proteins which were stable (but different from normal) in stable phase of CML. At the onset of blast crisis, this pattern changed. Selected few proteins emerged as markers for irreversible escalation of the disease. Some significantly decreased, and some increased. This was common to all patients. (Only carefully prepared mature granulocytes were compared.)

CONCLUSIONS

A pattern of proteins separated by our method using HPLC and SDS electrophoresis was shown to be common and very stable for normal granulocytes (male and female, ages 19 to 70; mature granulocytes from normal peripheral blood served as controls). For CML patients this pattern is different and varies with the stage of the disease, with significant changes at the onset of blast crisis.

REPORT DATE: 06/13/91

WORK UNIT # 1639-86

DETAIL SUMMARY SHEET

TITLE: Characterization of Human Antineutrophil Antibodies

KEYWORDS: neutropenia, anti-neutrophil, autoantibodies

PRINCIPAL INVESTIGATOR: Wright, Daniel LTC MC
ASSOCIATES: Hartman, Kip MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Mar 1986

FUNDING: Current FY: \$ 445 Previous FYs: \$ 0 Total: \$ 445

STUDY OBJECTIVE

To characterize the neutrophil antigens recognized by naturally occurring anti-neutrophil antibodies in autoimmune neutropenia.

TECHNICAL APPROACH

Sera from patients with neutropenia of suspected autoimmune origin are screened for the presence of anti-neutrophil antibodies. Further studies are then performed to further characterize these antibodies, including Western blotting, affinity chromatography separation of suspected autoantibodies, and immunofluorescence studies of autoantibody activity.

PRIOR AND CURRENT PROGRESS

To date, 63 patients have been identified by the screening assay as having an increased amount of anti-neutrophil antibody in their serum, and additional blood has been collected from three of these patients for further study. Since this is a blood collection study only, there have been no unexpected or adverse reactions, and no patients have withdrawn from study. There has been no direct benefit to patients other than diagnostic information provided to the clinicians regarding anti-neutrophil antibody status.

CONCLUSIONS

Autoantibodies specific for the neutrophil adhesion glycoprotein complex CD11b/CD18 were identified in the sera of several patients with autoimmune neutropenia. These autoantibodies have been found to alter certain neutrophil adhesion and opsonin receptor functions in vitro. Further studies are needed to determine the clinical significance of these findings.

REPORT DATE: 09/09/91

WORK UNIT # 1650-87

DETAIL SUMMARY SHEET

TITLE: Exploratory Dose Finding Study to Assess the Efficacy and Safety of Intravenous AHR 11190B (Zacopride Hydrochloride) in the Prevention of Cisplatin-Induced Emesis

KEYWORDS: Zacopride Hydrochloride, IND, drug

PRINCIPAL INVESTIGATOR: Lombardo, Fredric MAJ MS

ASSOCIATES: Adams, Jonathan DCR PHS; Knight, Robert LTC MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Hematology-Oncology Service

APPROVAL DATE: Nov 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the efficacy and safety of single doses of Zacopride Hydrochloride in the prevention of cisplatin-induced emesis, and to investigate the dose-response effect of Zacopride Hydrochloride for prevention of emesis caused by cisplatin.

TECHNICAL APPROACH

Protocol outline methodology. A particular dose of Zacopride is given 30 minutes prior to cisplatin infusion. If patients have six or more emetic episodes, Zacopride would be considered a filum, and other antiemetics will be administered.

PRIOR AND CURRENT PROGRESS

The protocol has been placed "on hold" by A.H. Robins Co., Richmond, VA, the holder of the IND. This is a multi-institutional study, and the first several patients placed on the study at other institutions elicited nausea and vomiting at the very low dose examined. Therefore, the company is in the process of amending the dosage scheme. We have not placed any patients on this study since we are awaiting the new dosage regimen. The protocol should remain open since it is only awaiting a dosage amendment. Communication with representatives from AHR indicates they are still very interested in WRAMC participation. The reason given for the long delay in making the dosage adjustment was the fact that the company has been recently reorganized under American Home Products, and there is new personnel in the Research Department.

CONCLUSIONS

Zacopride is still considered one of the most interesting new antiemetics. It is mostly a serotonin antagonist and will offer our patients an advantage once the dosage regimen is cleared.

REPORT DATE: 06/10/91

WORK UNIT # 1656-88

DETAIL SUMMARY SHEET

TITLE: Magnetic Resonance Imaging in the Staging and Evaluation of Response to Therapy in Small Cell Carcinoma of the Lung

KEYWORDS: MRI, small cell carcinoma, conventional staging

PRINCIPAL INVESTIGATOR: Burrell, Linda MAJ MC

ASSOCIATES: Perry, James MAJ MC; Lee, Nicole CPT MC

DEPARTMENT: Department of Medicine

SERVICE: Hematology-Oncology Service

STATUS: Ongoing

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare conventional staging (CS) to a single MRI imaging study for detection of extrathoracic metastases of small cell lung cancer; to compare CS versus MRI in assessing response of the disease to therapy; and to do a cost comparison of CS versus MRI.

TECHNICAL APPROACH

MRI protocol will observe spine, head, pelvis and femur as compared to conventional staging methods.

PRIOR AND CURRENT PROGRESS

Thirty-seven patients have been enrolled. The plan is to finish the study at 40 patients. To date, there have been no adverse reactions to this study. The benefit of this study is complete staging.

CONCLUSIONS

MRI identified more patients with extensive disease than did CS in this study. In two patients who had early progression, the site of extrathoracic disease was initially identified solely by MRI. MRI can be accomplished as a single study, was more convenient, and was well tolerated by all patients.

REPORT DATE: 06/22/91

WORK UNIT # 1657-88

DETAIL SUMMARY SHEET

TITLE: Long Term 5-FU Infusion for Recurrent Head and Neck Cancer, A Phase II Pilot Study

KEYWORDS: 5-fluorouracil, cancer, continuous infusion

PRINCIPAL INVESTIGATOR: Ward, Frank MAJ MC

ASSOCIATES: Lombardo, Frederick MAJ MC; Cobb, Patrick CPT MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Jun 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 13,650 Total: \$ 13,650

STUDY OBJECTIVE

a) Assess effectiveness of a continuous infusion of 5-FU in patients with recurrent head and neck cancer; and b) Assess the toxicity of a continuous infusion of 5-FU in patients with recurrent head and neck cancer.

TECHNICAL APPROACH

All adult patients with recurrent head and neck cancer who meet the eligibility requirements and consent to the protocol will have a central venous catheter placed (if one is not already in place) and will be subsequently treated with 24 hour per day continuous infusion 5-FU at 300 mg/m²/day dose, along with oral vitamin B6 to reduce the skin toxicity of the drug (in regard to hand-foot reaction). The drug will be continued in the absence of tumor progression or serious toxicity.

PRIOR AND CURRENT PROGRESS

Five patients have been accrued to this study. Toxicities observed are: skin rash, grade 1, two patients; mucositis, grade 1, one patient; lip ulceration, drug-related versus HSV, one patient; and palmar-plantar dysesthesia, grades 1 and 2, three patients. Only one patient required a dose reduction and delay in therapy (25% dose reduction with 1 week therapy delay) for toxicity (mucositis, rash). There were no objective responses among the five patients. There were no unexpected or serious toxicities. Median duration of time on study was 1.5 months, with a range of .25 to 7.5 months. Therapy was discontinued for disease progression or the development of disease-related complications. No patients were withdrawn for treatment-related toxicity. Of the five patients accrued to this study to date, three were enrolled in the last year.

CONCLUSIONS

Continuous infusion 5-fluorouracil is well tolerated by patients with recurrent head cancer. Patient accrual should continue to better define the clinical utility of this approach in recurrent head and neck cancer patients, a very poor prognostic group.

REPORT DATE: 07/19/91

WORK UNIT # 1658-88

DETAIL SUMMARY SHEET

TITLE: Verification of the Heterogeneity of Lupus Anticoagulant Using Purified IgG and IgM from Patients with Lupus Anticoagulant

KEYWORDS: lupus anticoagulant, cardiolipin antibody

PRINCIPAL INVESTIGATOR: Alving, Barbara LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To obtain blood from patients who have a lupus anticoagulant for the purpose of purifying and characterizing the antiphospholipid activity as being in the IgG or IgM fraction.

TECHNICAL APPROACH

IgG and IgM will be purified by column chromatography using DEAE cellulose from patient plasma.

PRIOR AND CURRENT PROGRESS

Ten patients have been studied on this protocol during the past year. Progress has been made toward purifying the IgG from the IgM fraction. New methods for the affinity purification of the antibodies using liposomes are being developed.

CONCLUSIONS

The heterogeneity of the antibodies is such that multiple patients need to be studied to determine the range of heterogeneity.

REPORT DATE: 10/07/91

WORK UNIT # 1659-88

DETAIL SUMMARY SHEET

TITLE: Antisickling Effect of Erythrocyte 2,3-DPG Depletion

KEYWORDS: sickle cell, 2,3-DPG, hemoglobin S

PRINCIPAL INVESTIGATOR: Kark, John COL MC

ASSOCIATES: Poillon, William PhD; Hicks, Cecil

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To evaluate the extent of the antisickling effect produced by in vitro depletion of erythrocyte 2,3-DPG (2,3-diphosphoglycerate) in red cells from patients with sickle cell disease; b) To measure the contributions made by each of several mechanisms for this effect; and c) To define optimum conditions for minimal levels of enzyme activators to achieve this effect.

TECHNICAL APPROACH

Small amounts of whole blood (30 ml) are drawn from patients with sickle cell disease or trait; the cells are washed, resuspended with activators of red cell 2,3-DPG phosphatase activity (glycolate or metabisulfite) or in control media, incubated for several hours, washed, resuspended in buffer and equilibrated with varying levels of po₂, and fixed. The percentage of sickled cells are compared for treated versus control samples. Oxygen affinity, 2,3-DPG, ATP, pH, and drug levels are measured in both types of cells.

PRIOR AND CURRENT PROGRESS

Conditions were found permitting reproducible depletion of 2,3-DPG in the treated cells, while the ATP of treated and control cells was stable, and the 2,3-DPG of the control cells was stable. Morphologic changes during hypoxia demonstrated a dose-response curve for percent sickling as a function of the level of 2,3-DPG. Percent sickling could be reduced by more than 50% in cells whose 2,3-DPG level was at the limits for detection. Analogs of glycolate are being tested at Howard University for their ability to deplete erythrocyte 2,3-DPG at sufficiently low doses for clinical use.

CONCLUSIONS

These experiments prove that 2,3-DPG plays a much more important role than previously known in the production of hemoglobin S polymer, the molecular basis for sickling. In addition to a better understanding of the pathophysiology of hemoglobin S, this implies that agents which deplete 2,3-DPG have the potential to function as powerful antisickling drugs.

REPORT DATE: 04/15/91

WORK UNIT # 1660-88

DETAIL SUMMARY SHEET

TITLE: Assessing the Usefulness of a Quantitative Measure of Mucosal
Neutrophils in Profoundly Neutropenic Patients

KEYWORDS: mucosal, neutrophil, neutropenia

PRINCIPAL INVESTIGATOR: Hargis, Jeffrey CPT MC

ASSOCIATES: Knight, Robert LTC MC; Wright, Daniel COL, MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Hematology-Oncology Service

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether quantitative measurements of oral neutrophils may provide information of clinical importance that supplements the information derived from blood neutrophil counts alone in defining the host defense defects of patients with profound neutropenia.

TECHNICAL APPROACH

Oral mucosal neutrophils are obtained by a daily saline mouthwash. The specimen is centrifuged and then stained with fluorescent acridine orange. Mucosal neutrophils are then counted by fluorescence microscopy in a hemocytometer chamber.

PRIOR AND CURRENT PROGRESS

Serial oral mucosal neutrophil counts have been obtained in eight patients given intensive chemotherapy. All eight patients developed profound neutropenia, and seven of eight patients had fever. The onset of fever has occurred on the day that the mucosal neutrophil count has fallen below 3% of pretreatment levels.

CONCLUSIONS

The mucosal neutrophil count is a noninvasive technique that accurately predicts the occurrence and timing of infectious complications in neutropenic patients.

REPORT DATE: 10/28/91

WORK UNIT # 1661-89

DETAIL SUMMARY SHEET

TITLE: Compassionate Study of Anagrelide

KEYWORDS: myeloproliferative, thrombocytosis, essential

PRINCIPAL INVESTIGATOR: Knight, Robert LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Terminated
APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This is a compassionate study utilizing Anagrelide in a patient with a disease marked by thrombocytosis.

TECHNICAL APPROACH

Anagrelide tablets are supplied by the Bristol-Myers Company and given to the patient on a daily schedule.

PRIOR AND CURRENT PROGRESS

This protocol has been administratively terminated.

CONCLUSIONS

This protocol has been administratively terminated.

REPORT DATE: 05/29/91

WORK UNIT # 1664-89

DETAIL SUMMARY SHEET

TITLE: A Phase II Evaluation of Suramin in Advanced Stage D2 Carcinoma of the Prostate

KEYWORDS: carcinoma, prostate, metastatic

PRINCIPAL INVESTIGATOR: Dawson, Nancy MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Completed
APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the efficacy and toxicity of the investigational agent suramin in metastatic prostate cancer, refractory to hormonal therapy.

TECHNICAL APPROACH

Suramin is administered intravenously by continuous infusion until a therapeutic blood level is achieved (range 4-21 days). Therapy is repeated every 6 to 8 weeks until complete remission or progressive disease.

PRIOR AND CURRENT PROGRESS

Protocol was a collaborative effort with the National Cancer Institute. Study closed July 1990. Total patients accrued - 54. Total accrued at WRAMC - 20. Total accrued at WRAMC since last report - 2. Two patients remain on therapy.

CONCLUSIONS

Suramin is an active agent in hormone-refractory prostate carcinoma. Drug levels must be monitored, as suramin is a major determinant of the type and severity of adverse effects observed in clinical use.

REPORT DATE: 08/14/91

WORK UNIT # 1665-89

DETAIL SUMMARY SHEET

TITLE: A Phase II Study of Simultaneous Radiotherapy and Cisplatin
Chemotherapy followed by 5FU and Cisplatin Chemotherapy in Patients
with Locally Advanced, Inoperable Squamous Cell Carcinoma of the Head
and Neck

KEYWORDS: radiotherapy, cisplatin chemotherapy

PRINCIPAL INVESTIGATOR: Perry, James MAJ MC

ASSOCIATES: Patow, Carl MAJ MC; Kaplan, Kenneth LTC MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Hematology-Oncology Service

APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Investigate the use of concurrent radiation and chemotherapy in patients with inoperable advanced head and neck cancer for response and disease-free survival.

TECHNICAL APPROACH

Administer concurrent cisplatin chemotherapy with standard radiotherapy to eligible patients, evaluate response, and follow longitudinally for disease-free survival. Population will be compared to historical controls and radiation therapy oncology group data base.

PRIOR AND CURRENT PROGRESS

Due to a continued lack of eligible patients, this study is being closed. While there is interest in continuing the study both at WRAMC and Wilford Hall Air Force Medical Center (where the protocol was also IRB-approved and activated), there are not enough patients for study accrual over a reasonable period of time. The concept of concurrent radiotherapy and chemotherapy continues to be actively investigated in head and neck cancer, with particular emphasis on sparing patients certain morbid surgical procedures (such as larynx preservation for advanced squamous cell carcinoma of the larynx). So, the objectives of this study were reasonable, but it appears that the patient base is lacking for even a single-arm Phase II study.

CONCLUSIONS

None.

REPORT DATE: 07/08/91

WORK UNIT # 1667-89

DETAIL SUMMARY SHEET

TITLE: Measurement of Protein S and Protein C in Anticoagulated Patients

KEYWORDS: protein S, protein C, Coumadin

PRINCIPAL INVESTIGATOR: Alving, Barbara LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Completed
APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The purpose of the study is to establish the levels of protein S and protein C, which are vitamin K-dependent proteins, in patients who take Coumadin but have not had venous thrombosis. These values will be used as a reference to assess patients who have had venous thrombosis and are taking Coumadin for underlying congenital deficiencies of protein S or C.

TECHNICAL APPROACH

Protein C is measured in clotting and chromogenic assays, and protein S is measured immunologically with Laurell rocket electrophoresis and in an ELISA. The values are compared to the Factor X antigen levels (ELISA) in the same patient and to the prolongation of the prothrombin time. From these studies, normal ratios of protein C and protein S to Factor X antigen will be established.

PRIOR AND CURRENT PROGRESS

No patients have been studied in the past year.

CONCLUSIONS

A deficiency of protein S or of protein C cannot be definitely diagnosed when patients are receiving Coumadin.

REPORT DATE: 08/08/91

WORK UNIT # 1668-89

DETAIL SUMMARY SHEET

TITLE: WRAMC 8904 High Dose Chemotherapy and Autologous Bone Marrow
Transplantation for Poor Prognosis Lymphomas, Phase II

KEYWORDS: autologous, bone marrow, chemotherapy

PRINCIPAL INVESTIGATOR: Perry, James MAJ MC

ASSOCIATES: Burrell, Linda MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) To test the feasibility of autologous bone marrow harvesting after initial tumor debulking with induction chemotherapy. 2) To determine the toxicity, time to marrow reconstitution, response rate, and time to treatment failure after high dose 3-drug consolidation with autologous bone marrow support.

TECHNICAL APPROACH

Eligible patients with relapsed lymphomas undergo conventional-dose salvage induction therapy. Those who achieve a response can undergo autologous bone marrow harvesting; followed by consolidation high-dose 3-drug chemotherapy using cyclophosphamide, etoposide, and BCNU; followed by infusion of the autologous bone marrow, which had been cryopreserved after harvesting. The patients are hospitalized until marrow engraftment.

PRIOR AND CURRENT PROGRESS

A total of five patients have been treated with autologous bone marrow transplant (ABMT) at WRAMC. Four patients were treated with a 4-drug regimen, with two toxic deaths reported. Other institutions found similar toxicity with this regimen. One patient relapsed and died of lymphoma, and one patient still remains in a complete remission. One patient has been treated with the modified regimen, which eliminated the ARA-C and decreased the BCNU to 600 mg. This modified regimen was tolerated well, without major toxicities being noted.

CONCLUSIONS

It was necessary to modify the study due to the high risk/benefit ratio. Using the 4-drug regimen there were two toxic deaths, one relapse, and one complete remission. Using the 3-drug regimen with decreased BCNU caused no major toxicities in the one patient. Other institutions using the previous protocol found similar toxic deaths and have also modified their protocol for ABMT in lymphoma.

REPORT DATE: 08/12/91

WORK UNIT # 1669-89

DETAIL SUMMARY SHEET

TITLE: WRAMC 8905: Chemotherapy with Autologous Bone Marrow Support for
Selected Advanced Solid Tumors, Phase II

KEYWORDS: bone marrow, chemotherapy, autologous

PRINCIPAL INVESTIGATOR: Burrell, Linda MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the toxicity, time to marrow reconstitution, response rate, and time to treatment failure for high-dose carboplatin, etoposide, and cyclophosphamide therapy with autologous bone marrow support for selected advanced solid tumors.

TECHNICAL APPROACH

Patients selected per eligibility requirements and presentation to Bone Marrow Transplant Conference. Patients undergo autologous bone marrow harvest with marrow separation and cryopreservation. They then receive 6 days of high-dose chemotherapy, followed by infusion of thawed autologous marrow. They are supported until marrow recovery in-hospital. At 60 days after transplant, they undergo reevaluation to assess response to the therapy and are then followed for clinical progression and/or late complications.

PRIOR AND CURRENT PROGRESS

A total of five solid tumor patients have been treated with autologous bone marrow transplant (ABMT) at WRAMC. Three patients on this regimen had no major toxicities, one is now being treated, and one patient died of an overwhelming fungal infection. Of the three patients who are status post ABMT, one was a partial remission and two were complete remissions at the 60 day evaluation. Another patient is scheduled to be placed on this regimen in August 1991.

CONCLUSIONS

The solid tumor ABMT regimen at WRAMC has been well tolerated, with no major toxicities. The one death occurred from an overwhelming fungal infection which manifested on day +1 and was unrelated to the chemotherapy regimen. The patient being treated now has tolerated the chemotherapy well, with only minimal nausea and vomiting. This study will continue with no changes in the chemotherapy dosages.

REPORT DATE: 07/01/91

WORK UNIT # 1670

DETAIL SUMMARY SHEET

TITLE: Anagrelide: Compassionate Use for an Individual Patient with
Thrombocytosis due to Myeloproliferative Disease

KEYWORDS: anagrelide

PRINCIPAL INVESTIGATOR: Perry, James MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Completed
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To achieve lowering of a patient's platelet count using an investigational agent, anagrelide.

TECHNICAL APPROACH

To administer anagrelide, obtained from Bristol-Myers, for use in an individual patient.

PRIOR AND CURRENT PROGRESS

One patient received the agent, anagrelide, from 31 Jul 89 until 14 Mar 90. The drug resulted in effective lowering of the platelet count due to the underlying myeloproliferative disease [chronic myelogenous leukemia (CML)]. The agent was discontinued when the patient developed acute myeloid leukemia (blast crisis of CML).

CONCLUSIONS

The agent, anagrelide, was safe and effective in this single patient.

REPORT DATE: 08/12/91

WORK UNIT # 1671

DETAIL SUMMARY SHEET

TITLE: A Prospective Study of the Use of Spinal Magnetic Resonance Imaging in
the Evaluation of Back Pain in Patients with Cancer

KEYWORDS:

PRINCIPAL INVESTIGATOR: Redmond, John COL MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Terminated
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol has been administratively terminated.

TECHNICAL APPROACH

This protocol has been administratively terminated.

PRIOR AND CURRENT PROGRESS

This protocol has been administratively terminated.

CONCLUSIONS

This protocol has been administratively terminated.

REPORT DATE: 06/10/91

WORK UNIT # 1672

DETAIL SUMMARY SHEET

TITLE: 5-Fluorouracil and Low Dose Leucovorin After Ultrasound Guided Laser Ablation of Colorectal Carcinoma Metastatic to the Liver

KEYWORDS: 5-fluorouracil, leucovorin, liver

PRINCIPAL INVESTIGATOR: Ward, Frank MAJ MC

ASSOCIATES: Dawson, Nancy LTC MC; Dachman, Abraham MD

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the effectiveness of 5-fluorouracil and low-dose leucovorin as therapy for metastatic colorectal carcinoma to the liver after laser ablation of the hepatic metastases, when compared to historical controls. Primary endpoint is survival. Disease-free interval, progression-free interval, and palliative effect of chemotherapy in conjunction with laser ablation are secondary endpoints.

TECHNICAL APPROACH

Patients who have undergone laser ablation of metastatic colorectal carcinoma to the liver will receive leucovorin (20 mg/m²/d) immediately followed by 5-fluorouracil (425 mg/m²/d) by rapid intravenous injection for 5 consecutive days. Courses will be repeated at 4 weeks, 8 weeks, and every 5 weeks thereafter in the absence of progressive disease or unacceptable toxicity. Survival will be calculated from the date of study entry. Doses will be modified for toxicity.

PRIOR AND CURRENT PROGRESS

No patients have been accrued to this study. This is a direct consequence of the failure to accrue any patients to the protocol employing laser ablation for colorectal carcinoma metastatic to the liver. The ability to accrue patients to the latter study was overestimated.

CONCLUSIONS

The small number of patients eligible for the laser ablation study over the last year were probably missed. Only 12 to 21% of patients with metastatic colorectal cancer would be expected to be eligible for that study, and most of that number would probably have a surgical attempt to resect the hepatic metastases. Nevertheless, improved publicity and other maneuvers to accrue patients to the laser study and this study are warranted.

REPORT DATE: 05/30/91

WORK UNIT # 1673

DETAIL SUMMARY SHEET

TITLE: Molecular Basis of the Maturation of Bone Marrow Granulocytes:
Isolation, Purification and Characterization of Granulocyte Maturation
Regulators from Normal Human Serum

KEYWORDS: granulocytes, maturation, regulator

PRINCIPAL INVESTIGATOR: Bednarek, Jana PhD
ASSOCIATES: Wright, Daniel COL MC; Ward, Frank LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 5,469 Previous FYs: \$ 0 Total: \$ 5,469

STUDY OBJECTIVE

To isolate, purify, and characterize the granulocyte maturation-inducing activity detected in normal human serum in our previous pilot study (Work Unit #1649-87).

TECHNICAL APPROACH

Chromatographic and electrophoretic procedures will be used to isolate, purify, and characterize the activity which we suspect is a protein or peptide. As the purification proceeds, at every step, we plan to assay for biological activity. This is accomplished in cultures of normal neutrophilic precursors from bone marrow. We will also attempt to use leukemic cell lines. When sufficiently purified, the molecule will be characterized by determination of molecular weight and amino acid composition. If it contains carbohydrates, we will determine its composition as well as its importance for biological activity/activities.

PRIOR AND CURRENT PROGRESS

We have carried the purification process of the maturation activity to a third step. Step one is accomplished by using DEAE fractogel displacement chromatography under controlled conditions at 4 degrees C in phosphate buffer pH 7.00. In step two, we also use DEAE fractogel but at pH 8.6 with Tween-20-0.02%. Most albumin and transferrin were removed, with only approximately 1% of protein remaining. Activity is stable for at least 2 months at 4 degrees C, but is lost on freezing. In the third step, we separate the protein by HPLC based on hydrophobicity. Acetonitrile and 0.1% trifluoroacetic acid were removed by freeze-drying. Sample was reconstituted for biological assay, but a considerable part of the activity was lost. On electrophoresis, three major bands appear; on overload and silver stain, several more are visualized.

CONCLUSIONS

Purification of maturation activity is proceeding, but we still do not have it pure enough to characterize the molecule. Preliminary assays of the activity show that leukemic cell lines, Red-3, and HL-60 can be stopped from dividing. Normal neutrophilic precursors, identified by CD-34 antigen, show reactions consistent with induction or recruitment by maturation factor.

REPORT DATE: 08/20/91

WORK UNIT # 1674

DETAIL SUMMARY SHEET

TITLE: Ifosfamide for Metastatic or Unresectable Primary Transitional Cell Carcinoma of the Urothelial Tract: A Phase II Pilot Study

KEYWORDS: ifosfamide, transitional cell, carcinoma

PRINCIPAL INVESTIGATOR: Reid, Thomas MAJ MC

ASSOCIATES: Ward, Frank LTC MC; Lombardo, Fred MAJ MSC

DEPARTMENT: Department of Medicine

SERVICE: Hematology-Oncology Service

STATUS: Ongoing

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of intravenous ifosfamide therapy in patients with transitional cell carcinoma of the urothelial tract who have failed standard therapy.

TECHNICAL APPROACH

Patients will be treated with ifosfamide 1.5 g/m²/d intravenous infusion over 2 hours per day for 5 days. Initial dose modifications will be made for previous pelvic irradiation and/or extent of previous chemotherapy. No modifications of the original protocol have been made.

PRIOR AND CURRENT PROGRESS

Last year was the first year of the protocol, and two patients were enrolled. There were no serious or unexpected adverse reactions. One patient progressed after his first course of therapy and was removed from further treatment. The other patient received two cycles and had stable disease. This patient became progressively cachectic after the second cycle and was removed from further therapy. Both patients have since died.

CONCLUSIONS

With only two patients enrolled to date, no definitive conclusions can be made about the efficacy of this drug. One patient had stable disease, while the other progressed early on. We anticipate higher accrual over the next year.

DETAIL SUMMARY SHEET

TITLE: WRAMC 9004 A Study of Interferon Alpha-2A in Combination with 5FU Plus Leucovorin in Metastatic or Recurrent Colorectal Cancer

KEYWORDS: colorectal cancer, interferon, 5FU/leucovorin

PRINCIPAL INVESTIGATOR: Weiss, Raymond MD

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Hematology-Oncology Service

APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To test the efficacy of the 3-drug regimen in 30 previously untreated metastatic or recurrent colorectal cancer patients.

TECHNICAL APPROACH

Non-randomized study in which all patients receive subcutaneous injections of interferon alpha, high dose IV leucovorin, and standard IV doses of 5FU every 3 weeks.

PRIOR AND CURRENT PROGRESS

Three patients have been registered to this study at WRAMC. One had progressive disease while on the treatment regimen. This patient was taken off the study and died shortly after from her rapidly progressing rectal cancer. An ADR had been reported for grade 4 GI toxicity in this patient. Two patients are currently being treated. There have been no adverse reactions in either of these patients. Neither of these patients have been on treatment long enough to be evaluated for response.

CONCLUSIONS

Study is ongoing; too early for evaluation.

DETAIL SUMMARY SHEET

TITLE: Detection of Lupus Anticoagulants in Patients with Anticardiolipin Antibodies

KEYWORDS: lupus anticoagulant, cardiolipin antibody

PRINCIPAL INVESTIGATOR: Alving, Barbara COL MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if patients with low, medium, or high anticardiolipin antibody titers also have a lupus anticoagulant as determined by two different phospholipid dilution assays.

TECHNICAL APPROACH

Plasma will be obtained from patients known to have anticardiolipin antibodies as determined in the Rheumatology Clinic at WRAMC under the direction of Dr. Joe Tesar. The APTT will be measured in the Coagulation Lab at WRAIR, and tests for lupus anticoagulants will be done utilizing the dilute phospholipid APTT or the RVVT.

PRIOR AND CURRENT PROGRESS

The collection of plasmas has just been initiated with three patients entered so far into the study.

CONCLUSIONS

More patients are needed before conclusions can be established.

DETAIL SUMMARY SHEET

TITLE: Studies of the Proliferation and Differentiation of Pluripotent Stem Cells and Committed Hematopoietic Precursors from Normal Bone Marrow Maintained in Continuous Long-term Cultures

KEYWORDS: stem cells, differentiation

PRINCIPAL INVESTIGATOR: La Russa, Vincent PhD
ASSOCIATES: Salvado, August COL MC; Knight, Robert LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Hematology-Oncology Service

STATUS: Ongoing
APPROVAL DATE: Oct 1982

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define mechanisms by which progenitor cells in the bone marrow replicate themselves and go on to form mature blood cells.

TECHNICAL APPROACH

The methods involved are: 1) the use of culture tubes and a defined media to study the behavior of stem cells for a period up to 8 weeks in culture; and 2) the use of clonal assays to quantitate the number of stem cells grown in culture.

PRIOR AND CURRENT PROGRESS

We have completed a pre-clinical evaluation of a novel immunotoxin, anti-CD33bR, for its potential use as an anti-leukemic purging agent for autologous bone marrow transplantation. We are also conducting investigations concerning guanine ribonucleotide metabolism and viral infections of bone marrow cells on the regulation of hematopoiesis.

CONCLUSIONS

The results from these studies will help us further understand mechanisms of blood cell production.

DETAIL SUMMARY SHEET

TITLE: Neutrophil Function in Patients with Diabetes Mellitus

KEYWORDS: diabetes mellitus, neutrophil, myeloperoxidase

PRINCIPAL INVESTIGATOR: Cross, Alan COL MC

ASSOCIATES: Glass, Allan COL MC; Duncan, William MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Infectious Disease ServiceSTATUS: Ongoing
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 7,236 Total: \$ 7,236

STUDY OBJECTIVE

To assess 1) neutrophil function of patients with diabetes mellitus and determine if impaired functional responses of diabetic neutrophils are related to a defect in the incorporation of exogenous inositol into hormonally sensitive phosphatidyl inositol pools, 2) lymphocyte function in diabetics by measuring expression of IL2 receptors, HLA-DR antigens, and IL2 production, and 3) neutrophil function by measuring calcium levels, and membrane depolarization.

TECHNICAL APPROACH

Since submitting an amendment, we have studied 27 patients and 20 control subjects. The most significant finding has been that the initial rates of superoxide formation in diabetics is twice that of controls; however, 10 minutes after stimulation, the neutrophils of diabetic patients generate levels of superoxide that are 25% that of controls. Resting, but not stimulated, intracellular calcium levels also differed between the two groups. The expression of IL2 receptors in response to some stimuli differed between the two groups. We are now correlating these differences with clinical parameters.

PRIOR AND CURRENT PROGRESS

We have focused our studies on the myeloperoxidase activity of neutrophils from Type I and Type II diabetic patients, since initial studies suggested a possible defect in normal intra-neutrophil myeloperoxidase activity in these patients. Since our last report, we have studied 13 additional Type I and II diabetic patients and 6 additional controls. We are currently analyzing the initial rates and "plateau" levels of MPO activity with regard to the degree of clinical control of their diabetes. Thus, the hemoglobin Alc, three recent blood glucose values, and clinical complications (e.g., nephropathy, retinopathy) will be correlated with the degree of MPO impairment.

CONCLUSIONS

To date, this study indicates no early signal transduction defect in neutrophils of patients with either Type I or II diabetes. There was no defect in membrane depolarization, intracellular acidification, or superoxide generation. There may, however, be a defect in the generation of MPO-mediated hypochlorous acid, a potent cidal mechanism of these cells. Analysis of our 31 patients and 14 controls should indicate if this approach is useful.

REPORT DATE: 05/30/91

WORK UNIT # 1965

DETAIL SUMMARY SHEET

TITLE: Treatment of Cutaneous Leishmaniasis with Pentostam

KEYWORDS: leishmaniasis, Pentostam, IND

PRINCIPAL INVESTIGATOR: Oster, Charles COL MC

ASSOCIATES: Magill, Alan MAJ MC; Gasser, Robert Jr. Lt Col MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Infectious Disease Service

APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) Provide continuous therapy for cutaneous leishmaniasis; 2) Determine peak and trough serum concentrations, and serum half-life, of Pentostam administered at a dose of 20 mg antimony (Sb)/kg body weight daily for 20 days; 3) Collect additional safety data on this dosing regimen; and 4) Compare 10 days therapy with 20 mg Sb/kg/day to 20 days therapy with 20 mg Sb/kg/day.

TECHNICAL APPROACH

Administration of Pentostam to patients diagnosed as having cutaneous leishmaniasis. Approximately five patients meeting the criteria for receiving Pentostam will be asked to donate blood in order to study the pharmacokinetics of this drug. This protocol will also provide for the randomization of patients to two groups: Group A will receive 20 mg Sb/kg/day for 20 days, and Group B will receive 20 mg Sb/kg/day for 10 days, followed by 50 ml DSW IV qd for 10 additional days. A total of 40 patients will be randomized. Five from each group will be asked to participate in the pharmacokinetic study.

PRIOR AND CURRENT PROGRESS

In calendar year 1990, six patients were treated on protocol. One patient was treated for visceral disease with a 30-day course; all others were treated for 20 days. No patients required early termination of therapy. Adverse reactions were mild, consisting of arthralgias in three, nauseas in three, and headache in one. Two patients had asymptomatic elevations in transaminases during therapy. Two patients have been seen in follow-up, and both remain disease free. No pharmacokinetics have been done to date.

CONCLUSIONS

Pentostam at a dose of 20 mg/kg/day for 20 days is efficacious in the therapy of cutaneous leishmaniasis. No conclusions can be drawn concerning the efficacy of a 10-day course of therapy.

REPORT DATE: 10/28/91

WORK UNIT # 1967

DETAIL SUMMARY SHEET

TITLE: Pharmacokinetics of Polyvalent Hyperimmune Globulin Directed Against Pseudomonas and Klebsiella

KEYWORDS: immunoglobulin, Pseudomonas, Klebsiella

PRINCIPAL INVESTIGATOR: McClain, Bruce LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Infectious Disease Service

STATUS: Ongoing
APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the pharmacokinetics of IVIG directed against gram negative germs in patients who are ill and in normal volunteers.

TECHNICAL APPROACH

Administer the immunoglobulin and bleed people, then subject the ELISA results to pharmacokinetic analysis.

PRIOR AND CURRENT PROGRESS

The hyperimmune immunoglobulin was administered to eight patients in the intensive care unit. Despite the presence of serious illness, seven demonstrated levels of antibodies to six antigens (three Pseudomonas and three Klebsiella) that were above initial pre-infusion values at the end of the 35 day study period. Paradoxically, most patients exhibited increasing levels of anti-Klebsiella and anti-Pseudomonas antibodies. There was only one case of colonization with these bacteria. Thus, infusion of these antibodies may induce the production of new antibodies by the patient. We no longer plan to accrue patients for this phase of the study. We do plan to continue the study by assessing if volunteers make type-specific antibody in response to IVIG infusion. This will be done under an amendment with a new consent form.

CONCLUSIONS

Infusions of hyperimmune immunoglobulin is well-tolerated in sick patients, and results in a level of specific anti-Klebsiella and anti-Pseudomonas antibodies above the pre-infusion baseline for up to 35 days. Interestingly, these antibodies may induce type-specific antibody production by the patient.

REPORT DATE: 04/16/91

WORK UNIT # 1969

DETAIL SUMMARY SHEET

TITLE: Protocol 188-803-Eprex Treatment Program for Anemia in AIDS Patients

KEYWORDS: anemia, AIDS, Zidovudine

PRINCIPAL INVESTIGATOR: Oster, Charles COL MC

ASSOCIATES: Ricks, Charles LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Infectious Disease Service

STATUS: Completed
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To provide erythropoietin (EPO) to alleviate the anemia caused by AIDS and/or Zidovudine (AZT) therapy and decrease transfusion needs.

TECHNICAL APPROACH

The patient must be at least 12 years old, have CDC defined AIDS, be anemic (HCT less than 30%), and have an endogenous EPO level of less than 500 ml/ml. Patients are treated with 4000 units subcutaneously 6 out of 7 days for 12 weeks with a target HCT of 38-40%. Dosage may be titrated up to 48,000 units per week to reach target HCT.

PRIOR AND CURRENT PROGRESS

Two patients have been enrolled in the study. One started in February 1990 but discontinued in March 1990 because of severe clinical deterioration; HIV wasting syndrome and advanced cachexia. The second patient was enrolled but moved out of the area and never received the drug. The drug has now been marketed by Ortho (Trade Name PROCRIT), and any remaining study drug was destroyed per instructions from the company. This is the final report.

CONCLUSIONS

The treatment IND protocol has been closed for enrollment. The drug is now FDA approved.

REPORT DATE: 04/16/91

WORK UNIT # 1970

DETAIL SUMMARY SHEET

TITLE: Treatment IND Protocol for the Use of Videx in Patients with AIDS who are Intolerant to Zidovudine and Patients Exhibiting Significant Deterioration while Taking Zidovudine

KEYWORDS: AIDS, intolerant, zidovudine

PRINCIPAL INVESTIGATOR: Oster, Charles COL MC

ASSOCIATES: Hicks, Charles LTC MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Infectious Disease Service

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To make DDI available to many patients with HIV infection who (1) have either developed intolerance of failed zidovudine therapy and (2) cannot enter the Phase II DDI program in the ACTG's due to protocol exclusion or geographic location.

TECHNICAL APPROACH

This study is an open label, uncontrolled evaluation of oral DDI administered every 12 hours at a dose based on the patient's weight: 35-49 kg = 167 mg bid, 50-74 kg = 250 mg bid, and greater than 75 kg = 375 mg bid.

PRIOR AND CURRENT PROGRESS

There have been six patients enrolled in the protocol. Two patients have had the medication stopped after about 1 month due to peripheral neuropathy, a commonly reported side effect. Three patients continue to take DDI; two of whom have had their dosage reduced because of peripheral neuropathy or weight loss. One patient was enrolled but expired before receiving the first dose.

CONCLUSIONS

This treatment IND protocol continues to be open for patients who cannot tolerate or have failed zidovudine therapy. Patient outcome and toxicity data continue to be forwarded to the company (Bristol), a requirement for further drug shipment.

REPORT DATE: 08/12/91

WORK UNIT # 1971

DETAIL SUMMARY SHEET

TITLE: Early Diagnosis of Tuberculosis Using the Polymerase Chain Reaction

KEYWORDS: tuberculosis, polymerase chain reaction

PRINCIPAL INVESTIGATOR: Sun, Wellington MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Infectious Disease Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 4,308 Previous FYs: \$ 0 Total: \$ 4,308

STUDY OBJECTIVE

To develop a polymerase chain reaction (PCR) assay applicable to clinical specimens at WRAMC and then to assess its specificity, sensitivity and overall feasibility as a clinical tool to diagnose tuberculosis. Because a quick test is especially useful in cases of smear negative but culture positive cases, this protocol specifically examined this population.

TECHNICAL APPROACH

Oligonucleotide primers were synthesized using known gene sequences from the TB genome. By a process of trial and error, using purified mycobacterial genomic DNA as templates, two pairs of nested primers (from Pab protein gene) were found to be specific for TB. They were then used on over 50 clinical specimens. PCR using nested primers can eliminate the necessity of doing confirmatory Southern blots and thus make the results of this test available in 24 hours.

PRIOR AND CURRENT PROGRESS

During this study it has been established that: 1) The sensitivity of PCR on specimens critically depends on proper and efficient extraction of template DNA; 2) A simplified procedure of boiling specimens, with the addition of a chelating agent, Chelex, can greatly simplify the extraction procedure; 3) Nested primer PCR's consistently and reproducibly amplify target DNA; and 4) Nested primer PCR's may dispense with confirmatory Southern Blotting.

CONCLUSIONS

Sequential nested primer PCR is 66% sensitive and 100% specific in diagnosis of TB directly from clinical specimens. Further improvements in sensitivity will depend on optimization of processing specimens to extract target genomic DNA.

REPORT DATE: 08/16/91

WORK UNIT # 8816

DETAIL SUMMARY SHEET

TITLE: Assessment of Risk Factors for HIV Infection Among AD U.S. Army
Personnel with Documented Recent HIV Antibody Seroconversion

KEYWORDS: HIV, seroconversion, risk

PRINCIPAL INVESTIGATOR: McNeil, John MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Infectious Disease Service

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To investigate behavioral and other determinants of HIV seroconversion among active duty male soldiers.

TECHNICAL APPROACH

Case control study, blinded, anonymous and confidential interview by civilian disease intervention specialists at 24 sites within CONUS.

PRIOR AND CURRENT PROGRESS

Although the study continued throughout fiscal year 1991, Operations Desert Shield/Storm limited the effort, especially at FORSCOM field sites. To date, 220 study subjects have been recruited and interviewed. Preliminary analyses of study data have been conducted, and results have been presented to medical professional and military leadership audiences. There are no adverse events to report. There have been no observable benefits to study participants, but data generated from this study is being used to refine educational interventions to prevent new HIV infections among active duty soldiers.

CONCLUSIONS

This study will continue under the present design until February 1992. Final analysis of study data and preparation of a manuscript for publication will occur during Spring 1992.

REPORT DATE: 07/29/91

WORK UNIT # 1152

DETAIL SUMMARY SHEET

TITLE: In Vitro Analysis of Removal of Radiocontrast Agents (RCA) by Artificial Membranes

KEYWORDS: dialysis, radiocontrast, transport

PRINCIPAL INVESTIGATOR: Gouge, Steven MAJ MC

ASSOCIATES: Moore, Jack LTC MC

DEPARTMENT: Department of Medicine

SERVICE: Nephrology Service

STATUS: Ongoing

APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,332 Total: \$ 1,332

STUDY OBJECTIVE

1) To study removal of radiocontrast agents (RCA) by three types of artificial membranes. 2) To determine performance curves depicting clearance as a function of operating parameters to assist in assessing optimal conditions for RCA removal.

TECHNICAL APPROACH

An in vitro system consisting of standard dialysis machines and solutions will be used. Test perfusates were made by adding urea and one of two RCA to normal saline. These solutions were run through three types of dialyzers to different flow and pressures to assess RCA clearance.

PRIOR AND CURRENT PROGRESS

RCA mass transport was measured with cuprophane (CU) and polyacrylonitrile (PA) dialyzers. Both Hexabrix and Renografin RCA were used. Clearance of Renografin exceeded clearance of Hexabrix in both types of dialyzers which is attributed to the lower molecular weight of the former. Clearance of both RCA's was affected by TMP in only PA dialyzers and is due to convective transport. Diffusive transport accounted for RCA removal in cuprophane dialyzers. PA dialyzers are best for removal of RCA.

CONCLUSIONS

Demonstration of optimum operational characteristics will allow us to embark on a prospective study in patients at high risk for RCA toxicity. A manuscript is under consideration by the editors of Blood Purification.

REPORT DATE: 09/20/91

WORK UNIT # 1155

DETAIL SUMMARY SHEET

TITLE: The Effect of Thyroid Hormone Administration in Acute Renal Failure

KEYWORDS: renal failure, thyroxine, dialysis

PRINCIPAL INVESTIGATOR: Moore, Jack LTC MC

ASSOCIATES: Johnson, John COL MC; Burman, Kenneth COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Nephrology Service

APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether patients with acute renal failure (ARF) have improved survival when treated with thyroxine (T4) compared to patients who do not receive T4; to determine whether T4 alters the severity of ARF; to assess the thyroid axis in patients with ARF; and to determine whether T4 effects severity and mortality of ARF in parallel, or are these effects disparate.

TECHNICAL APPROACH

Adults with renal failure are stratified into two groups based on entry serum creatinine and urine output. They then receive either T4 or placebo in a double blind, placebo controlled study. Thyroid hormones are measured at intervals, and renal function is assessed. Data are analyzed in context with survival variables, thyroid function parameters, and dialysis requirements.

PRIOR AND CURRENT PROGRESS

Three patients have been entered into the study during the period it has been active. All of them completed the study successfully, and no patient sustained any event which could be attributed to study participation. This protocol was approved by 7th MEDCOM for use in case casualties received in Europe from the Persian Gulf War. None were. We are in the process of completing an amendment to the study which would allow us to include recipients of kidney transplants, since patient accrual has been extremely difficult.

CONCLUSIONS

None. Patient accrual continues.

REPORT DATE: 03/15/91

WORK UNIT # 1156

DETAIL SUMMARY SHEET

TITLE: Retrospective Analysis of the Use of Renal Ultrasound at Walter Reed
Army Medical Center

KEYWORDS: ultrasound, kidney, obstruction

PRINCIPAL INVESTIGATOR: Welch, Paul MAJ MC

ASSOCIATES: Lockard, Jerry MAJ MC; Moore, Jack Jr. LTC MC

DEPARTMENT: Department of Medicine

SERVICE: Nephrology Service

STATUS: Ongoing

APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,131 Total: \$ 1,131

STUDY OBJECTIVE

1) To survey the application of diagnostic ultrasonography at WRAMC by all requesting physicians. 2) To classify as standard or non-standard the indications for performing the sonogram, and to determine the relative frequency of abnormal versus normal results based on this distinction.

TECHNICAL APPROACH

All ultrasound reports in 6-month increments are collated, and the appropriate records are reviewed. Information from the records are then categorized into a) the indication for the ultrasound, b) the type of requesting physician, and c) the result of the ultrasound. A and C are subclassified into different strata which assist in data analysis. Data are then analyzed in a matrix format.

PRIOR AND CURRENT PROGRESS

Data analysis on the first 101 charts revealed 75% of the studies have been abnormal, with hydronephrosis and cysts being the most common abnormalities. 56% of the studies were done for standard indications, while 44% were performed for non-standard indications. Nephrologists, urologists, general internists, and general surgeons have different indications for ordering ultrasounds. The final 201 charts have been reviewed and are in data analysis at this time. The above invgator and associates that are listed will continue the analysis and manuscript preparation.

CONCLUSIONS

No conclusions can be reached. Data collection and analysis is continuing.

REPORT DATE: 04/01/91

WORK UNIT # 1157

DETAIL SUMMARY SHEET

TITLE: Effects of Thyroid Hormone and Thyrotropin (TSH) on Cultured Kidney Cells: Modulation of ANP Receptors and Epithelial Function

KEYWORDS: ANP, thyroid hormone, kidney

PRINCIPAL INVESTIGATOR: Moore, Jack LTC MC

ASSOCIATES: Tseng, Yueh-Chu PhD; Wartofsky, Leonard COL MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Nephrology Service

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 7,796 Total: \$ 7,796

STUDY OBJECTIVE

To determine whether the number or binding affinity of ANP receptors on renal cells is affected by incubation of such cells with ranging concentrations of thyroid hormone and thyroid hormone-depleted media; to correlate any changes with post-receptor and functional events.

TECHNICAL APPROACH

Rat papillary collecting duct cells (PCDC) were obtained as a gift from Dr. John Schwartz, Boston University. The ANP receptor in these cells was identified and characterized under control conditions, and in cells grown in T3-free media and media enriched with T3. The ANP receptor was characterized using hot and cold ANP. Guanylate cyclose (cyclic G) was measured using kit.

PRIOR AND CURRENT PROGRESS

PCDC exhibited very low specific binding at 37 and 25 C. At 4 C, a receptor Kd of 11nM and 1,500,000 binding sites/cell were identified. When cells were grown in T3-free media, or media enriched with T3, no change in specific binding was noted. ANP did produce significant changes in cyclic GMP; however, T3 did not effect cyclic G levels.

CONCLUSIONS

Any thyroidal influence on the renal cellular response to ANP is not mediated directly by changes in the number or binding affinity of ANP receptors in the PCDC model. A manuscript describing these findings is in preparation.

REPORT DATE: 06/17/91

WORK UNIT # 1158

DETAIL SUMMARY SHEET

TITLE: Tumor Necrosis Factor and Interleukin-1 Levels in Patients with Systemic Lupus Erythematosus

KEYWORDS: lupus, tumor necrosis factor, lupus nephritis

PRINCIPAL INVESTIGATOR: Welch, Paul MAJ MC

ASSOCIATES: Moore, Jack LTC MC; Strickland, Roger MAJ MC

DEPARTMENT: Department of Medicine

SERVICE: Nephrology Service

STATUS: Ongoing

APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,463 Total: \$ 1,463

STUDY OBJECTIVE

To correlate clinical markers of systemic lupus erythematosus (SLE) disease activity with levels of tumor necrosis factor (TNF) and interleukin-1 (IL-1).

TECHNICAL APPROACH

Part A: Patients with SLE with and without lupus nephritis will be prospectively recruited from the Rheumatology and Nephrology Clinics. Clinical parameters for disease activity will be correlated with TNF and IL-1 levels measured by RIA. Part B: Patients with SLE and sera stored in the Rheumatology sera bank will have TNF levels correlated with clinical disease activity retrospectively.

PRIOR AND CURRENT PROGRESS

Nine patients have been recruited for Part A (five this year). Patient recruiting is progressing slower than anticipated. Stored sera for Part B is available and can be measured when Part A recruiting is finished. No adverse reactions or benefits to patients have occurred.

CONCLUSIONS

None at this time.

REPORT DATE: 08/21/91

WORK UNIT # 1160

DETAIL SUMMARY SHEET

TITLE: Hemodynamic and Renal Response in the Rate to Hemorrhagic Hypotension in the Presence of ANF Antibody and in the Presence of Thiorphan, A Selective Metalloendoprotease Inhibitor

KEYWORDS: kidney, shock, atrial natriuretic

PRINCIPAL INVESTIGATOR: Yuan, Christine CPT MC

ASSOCIATES: Pamnani, Motilal, PhD; Moore, Jack Jr. LTC MC

DEPARTMENT: Department of Medicine

SERVICE: Nephrology Service

STATUS: Ongoing

APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 218 Previous FYs: \$ 17,513 Total: \$ 17,731

STUDY OBJECTIVE

To evaluate the physiologic role of atrial natriuretic factor (ANF) in hemorrhagic hypotension, and to assess the effects of exogenously administered ANF and/or Thiorphan (a selective metallendoprotease inhibitor which inhibits the catabolism of ANF) on renal function during hemorrhagic shock.

TECHNICAL APPROACH

Male Wistar rats, anesthetized with pentobarbital sodium, underwent hemorrhage to MAP=50 using a Wiggers-Jamson method. Hypotension was maintained for 3 hours. Inulin clearance, urine sodium excretion, c-GMP excretion, urine output, and plasma renin activity and immunoreactive ANF levels were measured hourly. Animals were then euthanized, and wedge sections of the right kidney were preserved in buffered formalin. Animals received ANF, Thiorphan, both ANF and Thiorphan, or the vehicle during the first hour of hemorrhage.

PRIOR AND CURRENT PROGRESS

The experiments outlined in the second part of the experimental protocol have been completed. A significant increase in urine output and inulin clearance was observed in animals receiving both ANP + Thiorphan and in those receiving Thiorphan alone vs. controls receiving the vehicle. Two abstracts have been published on the results of this work, and a paper has been submitted to the American Journal of Physiology. One hundred rats were approved for the protocol and have been used. There have been no findings that would preclude the use of animals.

CONCLUSIONS

1) ANP and Thiorphan, given in combination, during hemorrhagic hypotension, produce an increase in urine output, inulin clearance, and cGMP excretion compared to controls. 2) ANP given alone during hemorrhagic hypotension, has no effect on urine output, inulin clearance, or cGMP excretion, despite high plasma levels.

REPORT DATE: 07/16/91

WORK UNIT # 1707

DETAIL SUMMARY SHEET

TITLE: Relationship Between Respiratory Control Mechanisms and Nocturnal Desaturation in Diffuse Pulmonary Fibrosis

KEYWORDS: fibrosis, sleep, respiratory control

PRINCIPAL INVESTIGATOR: Rajagopal, Krishnan LTC MC
ASSOCIATES: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Feb 1981

FUNDING: Current FY: \$ 4,291 Previous FYs: \$ 6,976 Total: \$ 11,267

STUDY OBJECTIVE

To examine the relationship between respiratory control mechanisms and sleep desaturation in patients with pulmonary fibrosis.

TECHNICAL APPROACH

Patients with well defined diffused pulmonary fibrosis will be included in the study, and their results will be compared to results from similar tests performed in a group of volunteer controls. Nocturnal polysomnography and hypercapnic ventilatory and occlusion pressure (P100) responses will be performed to quantitate respiratory control mechanisms and nocturnal desaturation. The SPSS statistical package will be used for evaluation of correlates and co-correlates.

PRIOR AND CURRENT PROGRESS

To date, 11 patients with restrictive pulmonary disease (RPD) have been evaluated. Results indicate that waking ventilatory function is preserved in this group of patients while sleep is impaired. The latter is evidenced by a decrease in total sleep time, a decrease in sleep efficiency, a decrease in percent stage 2, 3/4, and REM sleep, and an increase in percent time awake and stage 1 sleep. The findings regarding sleep were greater for RPD patients with waking hypoxia ($PaO_2 < 80$ mmHg) compared to the non-hypoxic RPD patients.

CONCLUSIONS

Awake ventilation is preserved in RPD patients; however, sleep is significantly impaired. Hypoxic RPD patients have greater sleep impairment than non-hypoxic RPD patients.

REPORT DATE: 08/21/91

WORK UNIT # 1711

DETAIL SUMMARY SHEET

TITLE: Pulmonary Function in Psoriatic Arthritis

KEYWORDS: psoriatic arthritis, respiratory, pulmonary function

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Completed
APPROVAL DATE: Mar 1981

FUNDING: Current FY: \$ 0 Previous FYs: \$ 157 Total: \$ 157

STUDY OBJECTIVE

To define the limits of lung function in patients with psoriatic arthritis by doing a complete pulmonary function evaluation in a group of subjects with this diagnosis.

TECHNICAL APPROACH

Lung function is being assessed by measuring air flow using spirometry, lung volumes by plethysmography, and gas exchange with diffusing capacity.

PRIOR AND CURRENT PROGRESS

We have enrolled 18 subjects, analyzed the data, and submitted a manuscript. The reviewers recommended that a control group be included. The analysis is pending.

CONCLUSIONS

Manuscript has been written and submitted. There are no pulmonary function findings that are specific to psoriatic arthritis.

REPORT DATE: 10/07/91

WORK UNIT # 1714

DETAIL SUMMARY SHEET

TITLE: Mechanisms Limiting Exercise Ventilation in Chronic Obstructive Lung Disease

KEYWORDS: exercise, ventilation, COPD

PRINCIPAL INVESTIGATOR: Dillard, Thomas MAJ MC

ASSOCIATES: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Sep 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 220 Total: \$ 220

STUDY OBJECTIVE

To determine factors that limit ventilation at maximum exercise in patients with chronic obstructive lung disease (COPD).

TECHNICAL APPROACH

Continuous physiologic measurements are made on a bicycle ergometer during graded resistance exercise, with esophageal balloon in place for the measurement of pleural pressure to determine the work of breathing.

PRIOR AND CURRENT PROGRESS

The data analysis for this study requires laborious manual conversion of data from analog tracings to digital format. This step is necessary to produce numeric values for the results. Further entry of new subjects into data collection has not been done during the past year. Progress in the past year has focused on conversion of analog data already collected.

CONCLUSIONS

Progress continues in the area of data conversion and data analysis.

REPORT DATE: 06/13/91

WORK UNIT # 1717

DETAIL SUMMARY SHEET

TITLE: Prediction of Maximum Exercise Response from Resting Pulmonary Function
in Patients with Chronic Obstructive Pulmonary Disease

KEYWORDS: exercise, ventilation, COPD

PRINCIPAL INVESTIGATOR: Dillard, Thomas MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: May 1985

FUNDING: Current FY: \$ 145 Previous FYs: \$ 945 Total: \$ 1,090

STUDY OBJECTIVE

To test the hypothesis that assessment of inspiratory function in addition to expiratory function can improve the prediction of the exercise response of patients with chronic obstructive pulmonary disease (COPD).

TECHNICAL APPROACH

To evaluate parameters of both inspiratory and expiratory function in COPD patients, and to perform exercise tests in this group. Using these variables, prediction formulae with the highest r^2 values will be identified for maximum exercise ventilation and oxygen consumption. Data will be collected through record review.

PRIOR AND CURRENT PROGRESS

Under this protocol, exercise data involving 30 patients and pulmonary function data involving 105 patients have been collected to date. Current efforts on this protocol are directed at analysis of data as an interim step. Collection of additional data may become necessary to complete the project. During this latest project year funding support for reprints was requested and processed by DCI for publication in the near future.

CONCLUSIONS

Work on this protocol continues. Additional publications are anticipated and a need for additional DCI support is expected.

REPORT DATE: 07/12/91

WORK UNIT # 1720

DETAIL SUMMARY SHEET

TITLE: Pilot Study On the Use of Conjunctival Oxygen Tension Monitoring in the Sleep Apnea Syndrome

KEYWORDS: oxygen, sleep apnea, conjunctival monitor

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC
ASSOCIATES: Mohr, Lawrence LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$11,332 Previous FYs: \$ 18,860 Total: \$ 30,192

STUDY OBJECTIVE

To compare conjunctival oxygen tension monitoring with ear oximetry in Black sleep apneic patients.

TECHNICAL APPROACH

Using polysomnography (PSG) we plan to compare the two devices. In that skin pigmentation affects oximetry, the conjunctival monitor should be a reliable index.

PRIOR AND CURRENT PROGRESS

We have studied 12 Black subjects and 5 White controls. The data suggest that pigment does not affect the pulse oximetry readings when compared to conjunctival oxygen. There were some technical problems with the study that we have not been able to resolve because of non-availability of the conjunctival lens. We would like to keep the study open in hopes of resolving these issues over the next 12 to 24 months.

CONCLUSIONS

Pulse oximetry measured with a finger probe does not appear to be affected by increases in skin pigmentation.

REPORT DATE: 08/26/91

WORK UNIT # 1721

DETAIL SUMMARY SHEET

TITLE: Comparison of Prepregnancy and Postpartum Fitness Levels: A Pilot Study

KEYWORDS: fitness, pregnancy, activity

PRINCIPAL INVESTIGATOR: South-Paul, Jeanette MAJ MC

ASSOCIATES: Tenholder, Michael COL MC; Rajagopal, Krishnan LTC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Completed
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 326 Total: \$ 326

STUDY OBJECTIVE

To assess whether women regain their prepregnancy level of fitness within 30 days after delivery, following an uncomplicated pregnancy.

TECHNICAL APPROACH

Prepregnancy fitness will be assessed via 1) pulmonary function and cycle ergometer measurement of maximal oxygen consumption, 2) body fat determination via skin impedance and skin caliper methods, 3) baseline activity assessment via Minnesota Leisure Time Activity Questionnaire, and 4) psychiatric assessment via a child psychiatrist. The above steps will be completed prior to becoming pregnant and again 30 days following delivery.

PRIOR AND CURRENT PROGRESS

Seventeen nonpregnant volunteers enrolled in the study. Fourteen conceived, but only eleven completed both prepregnancy and follow-up (postpartum) testing. Weight, percent body fat, recall energy expenditure, and exercise responses to a stage 1, graded cycle ergometer exercise test were determined in these 11 subjects. Subject characteristics were compared by the Student's t test and differences across workloads and time were determined by analysis of variance with repeated measures.

CONCLUSIONS

Prepregnant weight was less than postpartum weight. Prepregnant energy expenditure and oxygen uptake were higher than postpartum period. Heart rate at 125 and 150 watts was lower prepregnancy compared to post pregnancy. These data support a detraining effect in early postpartum period. Whether this detraining is an inevitable factor associated with pregnancy or whether exercising throughout prepregnancy can ameliorate the decline in aerobic capacity postpartum is uncertain.

REPORT DATE: 04/03/91

WORK UNIT # 1724

DETAIL SUMMARY SHEET

TITLE: Mechanisms of Hypoxia During Simulated Air Travel in Patients with Chronic Obstructive Pulmonary Disease

KEYWORDS: hypoxia, COPD, emphysema

PRINCIPAL INVESTIGATOR: Dillard, Thomas MAJ MC

ASSOCIATES: Berg, Benjamin CPT MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Pulmonary Disease Service

APPROVAL DATE: Jan 1988

FUNDING: Current FY: \$ 97 Previous FYs: \$ 1,882 Total: \$ 1,979

STUDY OBJECTIVE

To describe the hypoxic response to altitude simulation in COPD patients, to identify determinants, and to compare treatment modalities.

TECHNICAL APPROACH

The methods use hypobaric hypoxia to produce hypoxemia. Determinant variables are measured using pulmonary function tests at ground level and hypobaric hypoxia. Treatment with oxygen by two modes of delivery are evaluated at altitude conditions.

PRIOR AND CURRENT PROGRESS

Data analysis and report preparation continue. Major reports to be submitted during the next year. Further data collection is not anticipated under this protocol.

CONCLUSIONS

None at this time.

REPORT DATE: 07/12/91

WORK UNIT # 1725

DETAIL SUMMARY SHEET

TITLE: Evaluation of Inspiratory Parameters in the Response to Inhaled
Bronchodilators

KEYWORDS: inspiration, mechanics, bronchodilators

PRINCIPAL INVESTIGATOR: Rajagopal, Krishnan LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To examine the effects of improvement in inspiratory measures on the relief in symptoms following the use of bronchodilator medication in patients with airflow obstruction.

TECHNICAL APPROACH

Pulmonary function tests will be performed before and after the inhalation of bronchodilator medications in patients with airflow obstruction. Inspiratory parameters will be examined, and changes in these parameters will be correlated with changes in subjective symptoms.

PRIOR AND CURRENT PROGRESS

A summer student began this study last fiscal year. She enrolled 20 subjects, and to date there is no evidence that inspiratory parameters correlate with symptoms.

CONCLUSIONS

No conclusions to date. Twenty additional subjects are needed to complete the study.

REPORT DATE: 07/08/91

WORK UNIT # 1726

DETAIL SUMMARY SHEET

TITLE: Physiologic Assessment of Exercise Limitation in Upper Airway
Obstruction

KEYWORDS: exercise, upper airway, lung mechanics

PRINCIPAL INVESTIGATOR: Rajagopal, Krishnan LTC MC
ASSOCIATES: Becker, Gregory CPT MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To examine the role of inspiratory muscle function in the limitation of exercise function.

TECHNICAL APPROACH

Patients with well defined upper airflow obstruction will have pulmonary function testing to determine resting inspiratory muscle function. Exercise testing will then be performed with monitoring of both inspiratory and expiratory airflow mechanics. The degree of inspiratory airflow reduction will be correlated with the degree of exercise limitation. Resting values will be used to derive predictors of exercise limitation.

PRIOR AND CURRENT PROGRESS

The project has resulted in good tracings being obtained. Isolated upper airway obstructions are quite uncommon, though four cases have been studied to date. Additional patients will be recruited, and the protocol will be completed in the next 12 to 18 months.

CONCLUSIONS

Work in progress. Will be completed with the addition of 9 more patients.

REPORT DATE: 06/06/91

WORK UNIT # 1728

DETAIL SUMMARY SHEET

TITLE: The Role of Respiratory Water Loss Without Heat Flux in
Exercise-Induced Asthma

KEYWORDS: exercise-induced asthma, respiratory heat loss, airway hyperreactivity

PRINCIPAL INVESTIGATOR: Phillips, Yancy LTC MC

ASSOCIATES: Argyros, Gregory CPT MC; Rayburn, Daniel PhD

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Completed
APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 388 Total: \$ 388

STUDY OBJECTIVE

To evaluate the effect of airway water loss in the absence of respiratory heat loss on bronchoconstriction in subjects with exercise-induced asthma. This indirectly implicates the mechanism of airway hyperreactivity in this population.

TECHNICAL APPROACH

Dry gas containing 5% CO₂ saturated with water at temperatures below 37 C is heated above body temperature. Specific combinations of water vapor and inspired temperature give conditions that are isenthalpic with alveolar gas (saturated at 37 C). The subject breathes the conditioned gas at 25 times FEV₁ for 6 minutes. PFT's are performed before and after, and decreases in airflow are measured. Each subject will undergo testing with different gas conditions on three days in random order.

PRIOR AND CURRENT PROGRESS

Inspired gas conditions of 37 C with 47 mmHg water vapor pressure; 56 C with 38 mmHg; and 78 C with 27 mmHg have the same heat content as fully-saturated air at body temperature. In four normal subjects hyperventilating at a minute ventilation of 30 times their FEV₁ for 6 minutes, expired temperatures at the mouth averaged 39, 42, and 43 C for the three inspired conditions. Retrotracheal esophageal temperatures did not fall in any subject, thereby demonstrating the absence of significant airway cooling. Ten subjects with exercise-induced asthma were tested with the same conditions. Baseline functions showed FEV₁ of 86 +/- 10% predicted (mean +/- s.d.), FVC 100 +/- 14% predicted and FEV₁/FVC 72 +/- 4%. The asthmatic subjects demonstrated post-challenge falls of FEV₁ of 2.8%, 5.7%, and 10.2% (P < 0.05 for 37 C compared to 78 C).

CONCLUSIONS

This study demonstrates that bronchospasm can be induced without any net respiratory heat loss or airway cooling and suggests that it is proportional to the amount of water lost from mucosal surfaces.

REPORT DATE: 05/28/91

WORK UNIT # 1729

DETAIL SUMMARY SHEET

TITLE: The Effect of Pre-Procedure Ipratropium or Metaproterenol by Metered Dose Inhaler on Pulmonary Function Following Fiberoptic Bronchoscopy

KEYWORDS: metaproterenol, ipratropium, bronchoscopy

PRINCIPAL INVESTIGATOR: Phillips, Yancy LTC MC

ASSOCIATES: Argyros, Greg CPT MC; Pike, James MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Pulmonary Disease Service

APPROVAL DATE: Jun 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare to placebo the use of either inhaled ipratropium bromide or inhaled metaproterenol as single agents prior to fiberoptic bronchoscopy. The treatments will be evaluated by their effect on the requirement for supplemental oxygen during the procedure and for their efficacy in preventing the expected decrement in pulmonary function following bronchoscopy.

TECHNICAL APPROACH

Patients undergoing elective fiberoptic bronchoscopy (FOB) are solicited for participation. Prior to FOB, pre- and post-screening spirometries using metaproterenol and ipratropium are completed. On the day of FOB, pre- and post-screening spirometries are completed using one of three inhalers. FOB is then done monitoring heart rate and oxygen saturation. A repeat screening spirometry is then completed following FOB. No modifications have been made to date.

PRIOR AND CURRENT PROGRESS

This study has now been completed. Thirteen subjects were added this past year, for a total of 39 as outlined in the original application. Two patients were withdrawn from the study over its entirety. Each had adverse effects associated with bronchoscopy but not related to protocol. No serious or unexpected adverse effects have been noted. The use of metaproterenol by metered dose inhaler prior to bronchoscopy promoted the maintenance of bronchial tone following bronchoscopy.

CONCLUSIONS

Post bronchoscopy maintenance of bronchial tone using metaproterenol beforehand suggests this should be used on a routine basis prior to bronchoscopy. The failure of ipratropium bromide to maintain bronchial tone is of concern and warrants further investigation. For now it should probably be avoided in this circumstance. Oxygen desaturation during bronchoscopy was not prevented by the use of these medications.

REPORT DATE: 08/05/91

WORK UNIT # 1730

DETAIL SUMMARY SHEET

TITLE: Characterization of Ventilatory Patterns, Ventilatory Requirements and Oxygen Consumption During Uncomplicated Labor in Normal Parturients

KEYWORDS: labor, oxygen, consumption

PRINCIPAL INVESTIGATOR: Phillips, Yancy LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Completed
APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 721 Total: \$ 721

STUDY OBJECTIVE

To measure the oxygen consumed, carbon dioxide produced, and ventilatory patterns of normal pregnant women in labor.

TECHNICAL APPROACH

Healthy women, aged 18 to 36, in the 38th to 41st week of gestation, will be recruited during a routine visit to OB Clinic. A baseline measurement of ventilatory parameters are made at rest. Repeat studies are performed (10 min procedure) during brief portions of stages I and II of labor.

PRIOR AND CURRENT PROGRESS

A total of 14 pregnant women were studied, and 9 of these were restudied during labor. Values obtained indicate that oxygen consumption goes up a mean of 21%, and minute ventilation goes up a mean of 58% in the transition from resting pregnancy to stage I of labor. These data allow predictive equations to be generated. These predictive equations may be useful to clinicians to determine which patients with cardiopulmonary limitations may labor successfully, which patients may require careful monitoring during a trial of labor, and which patients should be sent right to C-section. A manuscript has been written and is being cleared by WRAMC for consideration for publication.

CONCLUSIONS

As above.

REPORT DATE: 09/26/91

WORK UNIT # 1732

DETAIL SUMMARY SHEET

TITLE: Pleural Pressure Measurements in Normal Healthy Volunteers During the Administration of Nasal Continuous Positive Airway Pressure (NCPAP)

KEYWORDS: nasal CPAP, pleural pressure, esophageal pressure

PRINCIPAL INVESTIGATOR: Derderian, Sarkis LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 818 Previous FYs: \$ 4,369 Total: \$ 5,187

STUDY OBJECTIVE

The objective of this pilot study is to quantify the increase in pleural pressure due to nasal continuous positive airway pressure (NCPAP). This will be accomplished by measuring pleural pressure at several levels of NCPAP in normal healthy volunteers.

TECHNICAL APPROACH

To measure pleural pressure at different levels of NCPAP using the esophageal balloon technique and, in addition, to continuously record chest/wall and abdominal motion.

PRIOR AND CURRENT PROGRESS

One subject was studied in order to standardize the procedure. Due to the lack of technical support we have not been able to proceed further. We anticipate completing this study within 18 months now that technical support is available. No data is yet available in the literature regarding this issue.

CONCLUSIONS

None to date.

REPORT DATE: 08/21/91

WORK UNIT # 1734

DETAIL SUMMARY SHEET

TITLE: The Effect of Face Mask CPAP on Radionuclide Ventilation Perfusion
Scanning of the Lung in the Setting of Postoperative Atelectasis

KEYWORDS: atelectasis, lung scanning, nasal CPAP

PRINCIPAL INVESTIGATOR: Phillips, Yancy LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Completed
APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,230 Total: \$ 1,230

STUDY OBJECTIVE

To determine the effect of CPAP on the clinical, roentgenographic and radionuclide perfusion scanning manifestations of postoperative atelectasis. The hypothesis is that the application of nasal CPAP will ameliorate both the perfusion and ventilation defects on lung V/Q scan. This would then imply that CPAP could increase the specificity of V/Q scans for pulmonary embolus.

TECHNICAL APPROACH

Patients undergoing elective upper abdominal surgery are recruited. PFT's are performed before surgery. If clinical atelectasis is present, the patient has PFT's, ABG, and lung scan. Patient is then randomized to routine care or nasal CPAP. After 6 hours, the ABG, PFT's and scan are repeated. Clearing of previous defects on lung scan are taken as a positive effect.

PRIOR AND CURRENT PROGRESS

No patients have been enrolled in the past year. Twenty-nine patients have been enrolled to date, and only one has completed the study. The current plan is to modify the protocol to look at patients with abnormal VQ scans and to use the CPAP as an intervention prior to angiography. The significant changes required to this protocol would be too extensive for an amendment. Therefore, this study is being closed at this time.

CONCLUSIONS

None.

REPORT DATE: 03/08/91

WORK UNIT # 1735

DETAIL SUMMARY SHEET

TITLE: Outcome of Cardiopulmonary Resuscitation in the Intensive Care Unit

KEYWORDS: CPR, Intensive Care Unit

PRINCIPAL INVESTIGATOR: Landry, Frank CPT MC

ASSOCIATES: Phillips, Yancy LTC MC; Parker, Joseph MD

DEPARTMENT: Department of Medicine

STATUS: Completed

SERVICE: Pulmonary Disease Service

APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the outcome of cardiopulmonary resuscitation (CPR) of patients hospitalized in the surgical and medical intensive care units (ICU). In addition, characteristics of those patients who died in the do-not-resuscitate (DNR) status will be compared to those undergoing resuscitation.

TECHNICAL APPROACH

We conducted a retrospective review of all death charts and charts of patients undergoing resuscitation in the ICU at Walter Reed over a 2 year period. Demographic and clinical information was abstracted, and characteristics of the code were obtained for all arrests.

PRIOR AND CURRENT PROGRESS

All 201 charts meeting the criteria of the study have been reviewed and analyzed. Since this study used a retrospective design, there has been no serious or adverse reactions as a result of the study.

CONCLUSIONS

CPR was performed in 114 patients, and an additional 87 patients died in the do-not-resuscitate status during a 2 year period. Although 50 (44%) of those undergoing CPR initially survived, only 6 patients (5%) survived to hospital discharge. Those dying in the do-not-resuscitate status tended to be older, with higher APACHE II scores.

REPORT DATE: 04/04/91

WORK UNIT # 1736

DETAIL SUMMARY SHEET

TITLE: Treatment of Pulmonary Sarcoidosis with High Dose Inhaled Triamcinolone Acetonide

KEYWORDS: sarcoidosis, triamcinolone acetonide, therapy

PRINCIPAL INVESTIGATOR: Poropatich, Ronald MAJ MC
ASSOCIATES: Phillips, Yancy LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of high dose inhaled triamcinolone acetonide compared with oral prednisone in the treatment of biopsy proven, symptomatic, pulmonary sarcoidosis with or without associated pulmonary symptoms.

TECHNICAL APPROACH

A prospective randomized double-blind, placebo-controlled study. Forty-four patients will be enrolled in the study and undergo laboratory evaluation comprised of biochemical testing and pulmonary function analysis, at initiation, and completion of the study period (duration 6 months). Monthly physician visits will be conducted to assess objective and subjective clinical response, monitor untoward side effects, and assess compliance with therapy. Three chest x-rays will be taken during the study period.

PRIOR AND CURRENT PROGRESS

Five patients are currently enrolled in the protocol comprising 2-5 months of study participation. There have been no untoward side effects noted and no patient withdrawals. Although data has not yet been statistically reviewed, objective and subjective improvements have been observed in both patients, with decreased pulmonary symptoms and increased pulmonary function tests.

CONCLUSIONS

Preliminary results are encouraging in that all patients have improved under therapy. Since all results are still blinded, no conclusion can be made yet regarding the efficacy of high dose inhaled triamcinolone acetonide in the treatment of pulmonary sarcoidosis.

REPORT DATE: 05/21/91

WORK UNIT # 1737

DETAIL SUMMARY SHEET

TITLE: Predicting Exercise Responses in COPD Patients

KEYWORDS: exercise, COPD, emphysema

PRINCIPAL INVESTIGATOR: Dillard, Thomas MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the accuracy of descriptive models for oxygen consumption and exercise ventilation in COPD patients. Descriptive models for these parameters were previously developed at WRAMC. These models use values from resting pulmonary function tests to predict the parameters at maximum exercise.

TECHNICAL APPROACH

Perform exercise testing of patients and measurement of resting lung function tests. Generate predicted values using previous descriptive models and compare to observed values using statistical methods.

PRIOR AND CURRENT PROGRESS

Fourteen patients have completed the protocol. No results have been tabulated or analyzed thus far.

CONCLUSIONS

This protocol is active in the data collection phase.

REPORT DATE: 08/01/91

WORK UNIT # 1738

DETAIL SUMMARY SHEET

TITLE: Incidence of Arrhythmias During Pentamidine Therapy

KEYWORDS: arrhythmia, pentamidine

PRINCIPAL INVESTIGATOR: Eliasson, Arn MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of arrhythmias during pentamidine therapy.

TECHNICAL APPROACH

Patients at WRAMC receiving IV or inhaled pentamidine will be evaluated prospectively for risk factors for arrhythmias. They will be followed with periodic EKG's and other cardiologic studies including echocardiograms and Holter monitors. Specific endpoints include changes in QT intervals and frequencies of arrhythmias correlated with the dose of pentamidine administered.

PRIOR AND CURRENT PROGRESS

EKG and Holter monitors have been purchased and made operational. Four patients with IV pentamidine and 8 patients with inhaled pentamidine have been enrolled.

CONCLUSIONS

Over the next 12 months, sufficient numbers of patients on inhaled pentamidine will likely have been accrued. Patients on the intravenous form of pentamidine appear to be very unusual and are admitted in irregular bursts. The completion point for these patients appears to be much more unpredictable.

REPORT DATE: 08/01/91

WORK UNIT # 1739

DETAIL SUMMARY SHEET

TITLE: VA Cooperative Study No. 316: Efficacy of Passive Immunization in the Prevention of Infection due to Klebsiella Pneumoniae and Pseudomonas Aeruginosa

KEYWORDS: antibody, Klebsiella, Pseudomonas

PRINCIPAL INVESTIGATOR: Eliasson, Arn MAJ MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of a polyclonal antibody preparation in the prevention of bacteremia and sepsis from Klebsiella and Pseudomonas.

TECHNICAL APPROACH

Patients admitted to the intensive care units who are likely to stay longer than 3 days, and who are not felt to be immediately preterminal, will receive the antibody preparation or a placebo in the form of albumin infusion. Endpoints will include blood cultures, other clinical parameters of infection, and death. This is a multicenter study involving 16 medical centers and anticipates an enrollment of 16,000 patients.

PRIOR AND CURRENT PROGRESS

In the fall of 1990, the clinical study coordinator resigned and left the protocol without the manpower necessary to enroll patients. Efforts to recruit a study coordinator are ongoing.

CONCLUSIONS

A fulltime Registered Nurse or Physician's Assistant to perform data collection is needed.

REPORT DATE: 09/23/91

WORK UNIT # 1740

DETAIL SUMMARY SHEET

TITLE: The Effect of Diltiazem on Pulmonary Gas Exchange in Patients with Chronic Obstructive Lung Disease at Rest, with Exercise, with Exposure to a Hypoxic Environment and during Sleep

KEYWORDS: Ca channel, COPD, gas exchange

PRINCIPAL INVESTIGATOR: Moores, Lisa CPT MC

ASSOCIATES: Phillips, Yancy LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the potential of calcium channel antagonists to blunt the pulmonary vasoconstrictive response to hypoxemia, thus lowering pulmonary vascular resistance, increasing ventilation-perfusion mismatching, and worsening hypoxemia.

TECHNICAL APPROACH

Prospective study in patients with severe airflow obstruction and mild hypoxemia -- all subjects undergo baseline studies of ABG, pulmonary function, resting cardiac output, and incremental cardiopulmonary exercise before and after two hours of acute administration of 60 mg diltiazem. Subjects are then randomly assigned to receive four weeks of either diltiazem or a placebo, 60 mg TID, at which time all tests are repeated two hours after a medication dose.

PRIOR AND CURRENT PROGRESS

Fourteen patients meeting the above criteria have been completely studied. Plans are to continue the study in an attempt to enroll more patients. In addition, we would like to look specifically at the cardiopulmonary effects of chronic diltiazem use during sleep, which have not been addressed yet.

CONCLUSIONS

Preliminary review of the complete data set in the first fourteen patients reveals that neither cardiac output, oxygen delivery, pulmonary function nor exercise performance were significantly effected by the acute administration of diltiazem. Similarly, chronic use of diltiazem did not effect any test of cardiopulmonary function.

REPORT DATE: 08/12/91

WORK UNIT # 1741

DETAIL SUMMARY SHEET

TITLE: Value of Lingular or Right Middle Lobe Lung Biopsy Vs. Upper or Lower
Lobe Lung Biopsy: An Autopsy Series

KEYWORDS: lung biopsy, pulmonary

PRINCIPAL INVESTIGATOR: Torrington, Kenneth LTC MC

DEPARTMENT: Department of Medicine
SERVICE: Pulmonary Disease Service

STATUS: Completed
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine uniformity of distribution of pulmonary pathologic processes based upon an autopsy series.

TECHNICAL APPROACH

N/A

PRIOR AND CURRENT PROGRESS

The Department of Pathology co-investigators decided the project was not worthwhile and declined to participate. Their participation would have been essential for the study to be successfully performed.

CONCLUSIONS

Were unable to begin study. Please close the protocol.

REPORT DATE: 08/16/91

WORK UNIT # 3220R

DETAIL SUMMARY SHEET

TITLE: An Experimental Model of Seronegative Lupus - A Study of Biological Role of Anti-Ro/SSA and La/SSB Antibodies

KEYWORDS: Anti-Ro/SSA, La/SSB, autoantibodies, sero-negative lupus

PRINCIPAL INVESTIGATOR: Tesar, Joseph MD

ASSOCIATES: Molina, Rudolph MD (Andrews AFB)

DEPARTMENT: Department of Medicine

SERVICE: Rheumatology Service

STATUS: Ongoing

APPROVAL DATE: May 1984

FUNDING: Current FY: \$ 9,204 Previous FYs: \$ 12,040 Total: \$ 21,244

STUDY OBJECTIVE

To develop an in vitro, experimental model of cutaneous manifestations of seronegative and neonatal lupus erythematosus using anti-Ro/SSA and La/SSB antibodies and a cultured, epithelial cell line, Hep-2. The study has clinical applications for all connective tissue diseases which are associated with Ro/SSA and La/SSB antibodies; such as, SLE, Sjogren's syndrome, and neonatal lupus erythematosus.

TECHNICAL APPROACH

The study is designed to define the effect of Ro/SSA and La/SSB containing antigen-antibody complexes on epithelial cells. Specifically, the release of Ro and La antibodies from epithelial cells is induced by various environmental agents, such as UV-radiation, heat exposure, etc. The complement fixing capacity and potential toxicity of Ro/SSA and La/SSB antigens complexed with the homologous antibodies isolated from SLE sera will be studied using immunofluorescent antibody techniques. An animal model of cutaneous and neonatal lupus will be developed using the above immunological reagents.

PRIOR AND CURRENT PROGRESS

1) Development of methods for isolation and quantitation of Ro and La antigens and antibodies. 2) Demonstration of release of Ro and La antigens from epithelial cell line by UV radiation and adenoviral agents. Formation of immune complexes in the presence of homologous antibodies was also demonstrated. 3) Immune complexes of IgG anti-SSA/SSB and anti-SSB/SSB composition activate human complement as demonstrated by fixation of C3 at the cell surface by immunofluorescent technique. 4) A new type of neonatal lupus with cutaneous manifestations associated with Sm and RNP antibodies was demonstrated. 5) Involvement of Ro/SSA and La/SSB antibodies was demonstrated in pathology of Sjogren's syndrome with CNS manifestations.

CONCLUSIONS

Complement activating immune complexes were induced on the surface of epithelial cells (Hep-2) by UV radiation and adenoviral agents in presence of anti-Ro and La nuclear antibodies and complement. A similar process is probably occurring in the skin of photosensitive individuals with SLE and neonatal lupus. Ro/SSA and La/SSB antibodies have a pro-inflammatory effect also in primary Sjogren's syndrome.

REPORT DATE: 06/20/91

WORK UNIT # 3703

DETAIL SUMMARY SHEET

TITLE: Autoimmune Phenomena in Patients with Inflammatory Osteoarthritis and Primary Nodal Osteoarthritis

KEYWORDS: autoimmunity, osteoarthritis

PRINCIPAL INVESTIGATOR: Strickland, Roger MAJ MC

ASSOCIATES: Riordan, Kathryn MD

DEPARTMENT: Department of Medicine

SERVICE: Rheumatology Service

STATUS: Ongoing

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 723 Total: \$ 723

STUDY OBJECTIVE

To determine the extent of autoimmune features with inflammatory osteoarthritis (OA) and primary nodal osteoarthritis.

TECHNICAL APPROACH

One hundred and forty Caucasian patients with primary nodal osteoarthritis or inflammatory OA will be screened with x-rays and laboratory tests for evidence of autoimmune disease.

PRIOR AND CURRENT PROGRESS

Patients with erosive osteoarthritis (8 women/4 men): 8/12 had evidence of sicca, 9/12 had thyroid abnormalities (Graves, thyroiditis, or hypothyroidism), and 4/12 had antithyroglobulin or thyroid antimicrosomal antibodies. Patients with osteoarthritis with predominant Heberden's nodes: 4/6 had sicca, and 2/6 had thyroid abnormalities. Patients with nodal osteoarthritis: 0/7 had sicca, and 1/7 had thyroid antibodies.

CONCLUSIONS

Patients with erosive osteoarthritis and Heberden's nodes may represent distinct subsets of osteoarthritis associated with immune aberrations with sicca features and thyroid abnormalities.

REPORT DATE: 06/20/91

WORK UNIT # 3704

DETAIL SUMMARY SHEET

TITLE: Iontophoresis Therapy for Rheumatoid Arthritis

KEYWORDS: iontophoresis, rheumatoid arthritis

PRINCIPAL INVESTIGATOR: Strickland, Roger MAJ MC

ASSOCIATES: Klipple, Gary MD; Mewshaw, Betsy RN, MSN

DEPARTMENT: Department of Medicine

SERVICE: Rheumatology Service

STATUS: Ongoing

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the efficacy and safety of an iontophoretic drug delivery system in the treatment with corticosteroids of synovitis of the hand and wrist joints in patients with rheumatoid arthritis.

TECHNICAL APPROACH

Patients with rheumatoid arthritis with active synovitis of the hand joints are randomized to receive corticosteroids into the affected joints with injection or iontophoresis or to receive sham injection or iontophoresis using normal saline.

PRIOR AND CURRENT PROGRESS

Eleven patients have been randomized and entered into the study, each with 3-5 joints treated. No results at this point. However, no adverse reactions have been encountered of any significance either from the iontophoresis or the injections. The patients are tolerating the procedures involved in the study very well.

CONCLUSIONS

No meaningful conclusions can be drawn yet.

REPORT DATE: 06/20/91

WORK UNIT # 3705

DETAIL SUMMARY SHEET

TITLE: Iontophoresis Therapy for Osteoarthritis

KEYWORDS: iontophoresis, osteoarthritis

PRINCIPAL INVESTIGATOR: Strickland, Roger MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Rheumatology Service

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the efficacy and safety of an iontophoretic drug delivery system in the treatment with corticosteroids of synovitis of the hand and wrist joints in patients with osteoarthritis.

TECHNICAL APPROACH

Patients with osteoarthritis with synovitis of the hand joints are randomized to receive corticosteroids into the affected joints with injection or iontophoresis or to receive sham injection or iontophoresis using normal saline.

PRIOR AND CURRENT PROGRESS

Two patients with osteoarthritis have been randomized and entered into the study. No results are available to provide conclusions at this time (i.e., not enough patients are studied as yet). No significant adverse reactions have been encountered.

CONCLUSIONS

Too early to draw conclusions.

REPORT DATE: 05/14/90

WORK UNIT # 3706

DETAIL SUMMARY SHEET

TITLE: Iontophoresis Therapy for Bursitis and Tendinitis

KEYWORDS: iontophoresis, bursitis, tendinitis

PRINCIPAL INVESTIGATOR: Strickland, Roger MAJ MC

DEPARTMENT: Department of Medicine

STATUS: Ongoing

SERVICE: Rheumatology Service

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the efficacy and safety of an iontophoretic drug delivery system in the treatment with corticosteroids of synovitis, bursitis, and tendinitis.

TECHNICAL APPROACH

Patients with bursitis and tendinitis are randomized to receive corticosteroids into the affected musculoskeletal area with injection of iontophoresis or to receive sham injection of iontophoresis using normal saline.

PRIOR AND CURRENT PROGRESS

Nine patients with a variety of soft issue rheumatism problems have been randomized and entered into the study. It is too early to draw meaningful conclusions and interpret the results. No adverse reactions of any significance have been reported.

CONCLUSIONS

Too early to draw conclusions.

REPORT DATE: 08/14/91

WORK UNIT # 3707

DETAIL SUMMARY SHEET

TITLE: A Study of Autoantibodies to Neutrophil Integrin Proteins in Patients with Rheumatoid Arthritis

KEYWORDS: autoantibodies, rheumatoid arthritis, integrins

PRINCIPAL INVESTIGATOR: Hartman, Kip MAJ MC

ASSOCIATES: Wright, Daniel COL MC; Klipple, Gary COL MC

DEPARTMENT: Department of Medicine

SERVICE: Rheumatology Service

STATUS: Ongoing

APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 2,329 Previous FYs: \$ 0 Total: \$ 2,329

STUDY OBJECTIVE

To determine the incidence of autoantibodies to the neutrophil adhesion glycoproteins CD11b/CD18 in patients with rheumatoid arthritis, and to investigate the correlation of these autoantibodies with the occurrence of infections.

TECHNICAL APPROACH

After consent, patients seen in the Rheumatology Clinic with the diagnosis of rheumatoid arthritis will be given a questionnaire, followed by a physician interview and a physical examination. Blood will be collected and sera evaluated for anti-neutrophil antibody activity by immunofluorescent flow cytometry; specific anti-CD11b/CD18 reactivity will be studied in an immunobead antigen capture assay. Sera positive for antibodies to these adhesion proteins will be further evaluated for effects on neutrophil adhesion and opsonin receptor functions.

PRIOR AND CURRENT PROGRESS

There have been 22 subjects enrolled to date, and there have been no patients withdrawn from the study. Data are currently being generated, and results are not yet evaluable.

CONCLUSIONS

None yet.

REPORT DATE: 07/18/91

WORK UNIT # 7136

DETAIL SUMMARY SHEET

TITLE: An Investigation of Frontal Lobe Mediated Knowledge Representation

KEYWORDS: cognition, frontal lobe

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) To develop face valid and psychometrically constrained tests of executive functions guided by a preliminary neuropsychologically derived information processing model; 2) To obtain normal control data; 3) To motivate a more detailed and complete neuropsychological model of executive (frontal lobe) functions based on observed brain-behavior relationships; 4) To develop guidelines for the care of individuals impaired with clinical or "subclinical" executive function deficits.

TECHNICAL APPROACH

Patients receive neurological and neuropsychological examinations at WRAMC and at NINDS, NIH.

PRIOR AND CURRENT PROGRESS

Ten patients have been entered into the study; four have had repeated testing at six months.

CONCLUSIONS

None; analyses not yet done.

REPORT DATE: 08/01/91

WORK UNIT # 7138

DETAIL SUMMARY SHEET

TITLE: Investigation of the Usefulness of Motor Evoked Potentials in Neurological Disorders

KEYWORDS: motor evoked potentials, magnetic, motor system

PRINCIPAL INVESTIGATOR: Jabbari, Bahman COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the yield of the newly invented magnetic evoked potentials in neurological disorders. This test can noninvasively measure the conduction times in the motor pathways of the brain and the spinal cord.

TECHNICAL APPROACH

Focal magnetic stimulation to the neural tissue is provided by a Nicolet 2000 unit. On each patient, the response will be recorded for the abductor pollicis and anterior tibialis muscles, and the nervous system will be stimulated at the wrist, Erb's point (brachial plexus, C6 cervical level, and scalp) at the region of hand and leg motor cortex. Absolute latency values for the peripheral and central potentials and the central conduction times will be compared with the normals for age and height provided in the literature. All patients will sign the informed consent prior to testing.

PRIOR AND CURRENT PROGRESS

A total of 200 patients were tested in different categories of neurological disorders. There were 46 patients with definite or probable multiple sclerosis, 14 with amyotrophic lateral sclerosis, 30 with peripheral neuropathy, 23 with osteoarthritis, 25 with intraspinal lesions, 10 with hydrocephalus, 40 with other neurological disorders, and 12 with hysterical paralysis. The incidence of MMEP abnormality was 88% in definite and 66% in probable multiple sclerosis, 95% in ALS, 80% in intraspinal lesions, 92% in peripheral neuropathies, 86% in hydrocephalus, and 0% in hysterical hemiparesis.

CONCLUSIONS

The results of our study so far demonstrate a high yield for MMEP in multiple sclerosis, amyotrophic lateral sclerosis and spinal cord pathology.

REPORT DATE: 03/21/91

WORK UNIT # 7140

DETAIL SUMMARY SHEET

TITLE: Evaluation of the Yield of HLA-Dr2 Antigen Testing in Narcolepsy and Excessive Daytime Sleepiness

KEYWORDS: narcolepsy, HLA DR-2, hypersomnolence

PRINCIPAL INVESTIGATOR: Jabbari, Bahman COL MC

ASSOCIATES: Duncan, Max MAJ MC

SERVICE: Neurology Service

STATUS: Completed

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 835 Total: \$ 835

STUDY OBJECTIVE

To determine the yield of HLA DR-2 in a population of patients referred for evaluation of excessive daytime sleepiness, and to identify clinical features which would predict DR-2 positivity.

TECHNICAL APPROACH

Patients who are referred for evaluation of excessive daytime sleepiness are asked history, examined, receive MSLOT (Multiple Sleep Latency Onset Test), and have blood drawn for HLA DR-2. Correlations are sought between the answer to historical questions, MSLOT results, and the result of blood testing for HLA DR-2.

PRIOR AND CURRENT PROGRESS

A total of 27 patients have been studied. Significant correlations ($p < 0.005$) were found between +HLA-DR2 and familial narcolepsy and with narcolepsy-cataplexy syndrome.

CONCLUSIONS

HLA-DR2 is positive in 100% of patients with narcolepsy-cataplexy syndrome and 100% of the patients with familial narcolepsy ($P < 0.005$).

REPORT DATE: 06/05/91

WORK UNIT # 7141

DETAIL SUMMARY SHEET

TITLE: Recombinant Beta Interferons as Treatment for Multiple Sclerosis: A
Multicenter Protocol

KEYWORDS: beta-interferon, multiple sclerosis

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the therapeutic efficacy of beta-interferon in multiple sclerosis.

TECHNICAL APPROACH

Patients will be administered six million units r-human beta-interferon intramuscularly weekly for two years and will then be followed for one to two years.

PRIOR AND CURRENT PROGRESS

A total of ten patients have been accrued into the study at WRAMC (over 80 patients in the multicenter consortium). There have been no adverse reactions.

CONCLUSIONS

Medication appears well tolerated to date. Study remains blinded.

REPORT DATE: 06/06/91

WORK UNIT # 7142

DETAIL SUMMARY SHEET

TITLE: Intramuscular Poly-ICLC and CCNU in the Management of Malignant Gliomas: An Open Trial

KEYWORDS: poly-ICLC, CCNU

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 295 Total: \$ 295

STUDY OBJECTIVE

To determine the toxicity and tolerance of low doses of poly-ICLC and CCNU in patients with malignant gliomas.

TECHNICAL APPROACH

Patients will be administered poly-ICLC at 10, 20, 50, and 100 mcgm/kg twice weekly for one year.

PRIOR AND CURRENT PROGRESS

Eight patients have been entered in the study at two poly-ICLC levels: 10 mcg/kg weekly and 10 mcg/kg twice weekly. There have been no significant adverse reactions or side effects to poly-ICLC. Two patients have dropped out of the study, three have died (mean survival, 53 weeks), and three are now stable on biweekly treatments (mean time since diagnosed, 54 weeks; range = 26-30 weeks).

CONCLUSIONS

Poly-ICLC 10 mcg/kg IM 1-2 times weekly is well tolerated by patients with malignant glioma.

REPORT DATE: 03/21/91

WORK UNIT # 7143

DETAIL SUMMARY SHEET

TITLE: Investigation of the Effectiveness of Nimodipine in Movement Disorders

KEYWORDS: nimodipine, movement disorder

PRINCIPAL INVESTIGATOR: Jabbari, Bahman COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effectiveness of calcium channel blocker nimodipine in movement disorders.

TECHNICAL APPROACH

Patients with involuntary movement disorders (chorea, myoclonus, dystonia, tremor) will be enrolled. Each patient will be videotaped prior to treatment. Nimodipine 30 mg will be prescribed qid for 10 days. Patient's improvement will be evaluated by a clinical rating scale and a second videotape. An unbiased observer will rate the tapes.

PRIOR AND CURRENT PROGRESS

So far, 10 patients have enrolled in this study. The type of movements included dystonia (torticollis), eight patients; myoclonus, one patient; and chorea, one patient. No significant improvement was noted.

CONCLUSIONS

In this study to date, a limited number of patients showed no response to nimodipine taken 120 mg daily.

REPORT DATE: 07/19/91

WORK UNIT # 7144

DETAIL SUMMARY SHEET

TITLE: A Controlled Efficacy Study of a Brief Multidisciplinary Brain Injury Rehabilitation Program in Moderately Head Injured Service Members

KEYWORDS: traumatic brain injury, moderate head injury

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine effectiveness and cost efficiency of a comprehensive TBI rehabilitation program, compared to one providing only counseling and support; To determine and quantify the short- and long-term neurologic and neuropsychologic consequences of moderate head injury in Army and its impact on some aspects of military performance; and to develop and test a relatively brief neuropsychologic screen that is sensitive to and predictive of effects of minor/moderate head injuries.

TECHNICAL APPROACH

Each subject will receive neurological, neuropsychological, psychiatric and medical rehabilitation; EEG and evoked potential, and neuroophthalmologic testing; physical and occupational therapy; clinical psychiatry interview; and an MRI. Following the comprehensive evaluation, patients will be randomly assigned to one of two treatment groups. Patients will then be returned to duty and followed.

PRIOR AND CURRENT PROGRESS

Obtained approval and funding for project from DVA. Funds are now being processed at USUHS. Personnel interviews underway. Evaluation instruments developed, and data entry forms prepared. Patient accruals to begin September 1991.

CONCLUSIONS

None at this time.

REPORT DATE: 07/17/91

WORK UNIT # 9200

DETAIL SUMMARY SHEET

TITLE: Anatomical and Functional Sequelae of Head Injuries Incurred in Vietnam

KEYWORDS: penetrating head injury, post traumatic epilepsy, neuropsychological

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: Neurology Service

STATUS: Ongoing
APPROVAL DATE: Jun 1980

FUNDING: Current FY: \$ 0 Previous FYs: \$ 6,875 Total: \$ 6,875

STUDY OBJECTIVE

To examine selected veterans who received head injuries in Vietnam, plus Vietnam veterans who received no head injuries as a control group.

TECHNICAL APPROACH

Each subject will receive a neurological exam, CT scan, speech pathology exam, motor exam, audiology exam, electrophysiology battery, and neuropsychological exam. In addition, an American Red Cross caseworker has interviewed each subject and family to complete a field study.

PRIOR AND CURRENT PROGRESS

Inpatient phase completed as of October 1984. Contact is maintained with VHIS subjects, and selected patients are reevaluated at WRAMC periodically. Analysis continues. See attached publication list. Recent analyses have entered on return to work after penetrating head injury. Fifty percent (50%) of our population is employed; return to work can be predicted from analysis of neurologic and cognitive status.

CONCLUSIONS

The VHIS data base represents an invaluable asset on computer tape and microfiche that will continue to provide room for analysis for years to come. While many of the questions posed in the original protocol have already been answered, new and often more exciting questions have arisen and will continue to arise as investigators explore the data.

REPORT DATE: 06/05/91

WORK UNIT # 9202

DETAIL SUMMARY SHEET

TITLE: Poly ICLC in the Treatment of Chronic Guillain-Barre Syndrome

KEYWORDS: Guillain-Barre, poly-ICLC, interferon

PRINCIPAL INVESTIGATOR: Salazar, Andres COL MC

SERVICE: Neurology Service

STATUS: Completed
APPROVAL DATE: Dec 1981

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the therapeutic usefulness of poly-ICLC in chronic Guillain-Barre syndrome.

TECHNICAL APPROACH

IV or IM administration of poly-ICLC weekly and then monthly for two or more months, depending on the initial response. Chronic administration as needed to maintain improvement.

PRIOR AND CURRENT PROGRESS

Poly ICLC has a beneficial effect in certain patients with chronic Guillain-Barre syndrome ("CRIP," chronic recurrent idiopathic polyneuritis). No additional patients were entered into the study in 1991.

CONCLUSIONS

Poly-ICLC may be beneficial in acute Guillain-Barre syndrome.

REPORT DATE: 08/26/91

WORK UNIT # 7515

DETAIL SUMMARY SHEET

TITLE: Comparison of Selected Anesthesia Agents With and Without Nitrous Oxide on Postoperative Nausea and Vomiting in Patients for Ambulatory Surgery

KEYWORDS: anesthesia agents, nausea, vomiting

PRINCIPAL INVESTIGATOR: Anderson, Craig MAJ AN

ASSOCIATES: Tague, Monica MAJ AN; Harper, William MAJ AN

DEPARTMENT: Department of Nursing

STATUS: Completed

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To find out if patients experience less nausea and vomiting when alfentanil or sufentanil are given with or without nitrous oxide.

TECHNICAL APPROACH

Anesthetic agents are randomly assigned according to group assignments: Group 1a-alfentanil and nitrous oxide; Group 1b-alfentanil without nitrous oxide; Group 2a-sufentanil and nitrous oxide; and Group 2b-sufentanil without nitrous oxide. The recovery room nurse in the Ambulatory Surgery Center records the incidence of nausea on the tracking form. No modifications have been made to the original proposal.

PRIOR AND CURRENT PROGRESS

Group 1a-15 patients, incidence of nausea and vomiting = 47%; Group 1b-15 patients, incidence of nausea and vomiting = 20%; Group 2a-16 patients, incidence of nausea and vomiting = 56%; Group 2b-19 patients, incidence of nausea and vomiting = 26%. There have been no serious or unexpected adverse reactions. No patients have withdrawn from the study. There have been no direct benefits to patients from this study. Because of Desert Storm deployments and PCS orders, no data has been collected since August 1990, and the study has been terminated.

CONCLUSIONS

The patients who received nitrous oxide had a greater incidence of nausea and vomiting. In order to control the separate statistical test Type I error rate at alpha = .01 and the Type II error rate at beta + 0.20 (80% power), the total sample size must be 160.

REPORT DATE: 03/25/91

WORK UNIT # 7517

DETAIL SUMMARY SHEET

TITLE: Physiological and Behavioral Responses of Preschool Children to a Stressful Medical Procedure

KEYWORDS: pediatric, behavior, stress

PRINCIPAL INVESTIGATOR: Leander, Deborah LTC AN

DEPARTMENT: Department of Nursing

STATUS: Completed
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To identify and collect data on preschool children's individual variations in patterns of responding to the stressful medical procedure of blood drawing by examining physiologic response in conjunction with measures of temperament, cognition, and parent/child coping.

TECHNICAL APPROACH

Prior to hospitalization, baseline physiologic and psychologic measures will be obtained from preschool children and parents. The child's responses will again be measured during blood drawing preparation and the blood drawing procedure. Two weeks post-hospital discharge, the family will complete a questionnaire.

PRIOR AND CURRENT PROGRESS

Due to scheduling difficulties encountered in the clinics, the researcher did not accrue any subjects at Walter Reed Medical Center.

CONCLUSIONS

None.

REPORT DATE: 06/01/91

WORK UNIT # 7518

DETAIL SUMMARY SHEET

TITLE: Do Preoperative Medications Affect Stress as Measured by Blood Glucose Levels and the State Trait Anxiety Inventory?

KEYWORDS: blood glucose, preoperative medications

PRINCIPAL INVESTIGATOR: Finnicum, Brenda CPT AN

DEPARTMENT: Department of Nursing

STATUS: Completed
APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if patients who receive preoperative medications have a change in stress levels as demonstrated by blood glucose measurement and the State Trait Anxiety Inventory.

TECHNICAL APPROACH

The patients who meet the criteria will have their blood sugar measured with an Accu-Check finger stick method before and after either: (1) receiving 5 mg of Valium, (2) receiving a placebo, or (3) receiving nothing. They will also complete the State Trait Anxiety Inventory just prior to having their blood sugar tested by the finger stick method.

PRIOR AND CURRENT PROGRESS

This study has been closed due to the lack of personnel to complete data collection. Eleven subjects were entered into the study.

CONCLUSIONS

No conclusions could be made, and no trends were identified.

REPORT DATE: 08/22/91

WORK UNIT # 7520

DETAIL SUMMARY SHEET

TITLE: The Relationship of the Sense of Coherence and Hardiness to the Nutritional Status of Anorectic Head and Neck Cancer Patients Currently Undergoing Radiation Therapy

KEYWORDS: hardiness, sense of coherence, nutritional status

PRINCIPAL INVESTIGATOR: Sarnecky, Mary LTC MC

ASSOCIATES: Forlaw, Loretta LTC AN

DEPARTMENT: Department of Nursing

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To investigate the relationship between the personality traits' sense of coherence and hardiness and the nutritional status of patients with head and neck cancer who are receiving radiation therapy.

TECHNICAL APPROACH

Experimental, correlational design study. Descriptive statistics will be used to summarize demographic information. Pearson product moment correlations will be used to explain the relationship between the sense of coherence, hardiness, and nutritional status, as well as the subscales of the Orientation to Life Questionnaire and the Health Related Hardiness Scale. The significant difference between the mean Body Mass Index at diagnosis and subsequent means for weeks 1-8 of radiation therapy will be assessed using the repeated measure t-test. Step-wise multiple regression will be applied to explain the statistical differences among variables.

PRIOR AND CURRENT PROGRESS

Forty patients have been enrolled in the study, with data analyzed as described above. No adverse reactions. No patients have withdrawn from the study. Six patients did not return the dietary intake form; however, this did not preclude their inclusion in study. No modifications have been made in the protocol.

CONCLUSIONS

Initial data suggests that patients with a high sense of coherence are more likely to maintain an adequate nutritional status.

REPORT DATE: 06/06/91

WORK UNIT # 9303

DETAIL SUMMARY SHEET

TITLE: Hospital Liquid Diet Evaluation

KEYWORDS: advanced liquid diet, standard liquid diet

PRINCIPAL INVESTIGATOR: Patterson, Richard LTC SP

SERVICE: Nutrition Care Directorate

STATUS: Ongoing
APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the acceptability of commercially produced advanced hospital liquid diets developed by the U.S. Army Natick Research, Development and Engineering Center in terms of overall appearance, flavor, consistency, textures, ease of sipping, and portion size.

TECHNICAL APPROACH

One hundred oncology, wired-jaw, or other inpatients with a diet order for an advanced liquid diet, will be used to evaluate the new menu of commercially produced hospital liquid diets. Patients who agree to participate in the study will be served the new advanced liquid diets instead of the standard liquid diets for three meals on one day only.

PRIOR AND CURRENT PROGRESS

No subjects who met the inclusionary criteria have volunteered to participate in the study. Zero subjects have been enrolled to date. There have been no serious or unexpected adverse reactions reported as a result of using these products. There are no direct benefits to subjects who participate in this study.

CONCLUSIONS

None at this time. Will continue to try to accrue patients.

REPORT DATE: 05/01/91

WORK UNIT # 4243

DETAIL SUMMARY SHEET

TITLE: The Effect of Vaginal Lubricants on Sperm Motility in the Postcoital Test

KEYWORDS: lubricants, sperm, motility

PRINCIPAL INVESTIGATOR: Opsahl, Michael LCDR MC USN

ASSOCIATES: Klein, Thomas COL MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

APPROVAL DATE: Feb 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 50 Total: \$ 50

STUDY OBJECTIVE

To determine sperm motility in vivo following the use of vaginal lubricants. The use of vaginal lubricants occasionally becomes an issue for infertile couples. We seek to determine if in vivo use of lubricants is likely to affect sperm-cervical mucus interaction.

TECHNICAL APPROACH

The sperm-cervical mucus interaction will be assessed after a standard postcoital test (PCT). The results of the tests will be compared from each couple after a PCT with, and one without, the use of vaginal lubricants. The physician will be blinded to the patient's use of lubricant.

PRIOR AND CURRENT PROGRESS

No patients have been accrued since the last Annual Progress Report. This is because of a shortage of personnel to conduct the study, and some question as to the length of the PI's remaining time on active duty. Both these issues have now been favorably settled, and it is hoped that patient accrual can resume and the study be completed.

CONCLUSIONS

None at present.

REPORT DATE: 05/09/91

WORK UNIT # 4258

DETAIL SUMMARY SHEET

TITLE: Detection of Herpes Simplex and Human Papillomaviruses in Exfoliated, Cervical Epithelial Cells by Means of In Situ Hybridization with Biotinylated DNA Probes

KEYWORDS: herpes simplex virus, human papillomavirus, in-situ hybridization

PRINCIPAL INVESTIGATOR: O'Conner, Dennis COL MC

ASSOCIATES: Marsella, Richard LTC MC; Woodward, Joan MAJ MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

APPROVAL DATE: Nov 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The detection of human papillomaviruses and/or herpes simplex virus genetic material in exfoliated cervical epithelial cells by in-situ DNA hybridization performed directly on Pap smears.

TECHNICAL APPROACH

An evaluation of women at risk for harboring herpes simplex and/or human papillomavirus infections was initiated. In this study, women in a variety of health status categories are being evaluated by means of Pap smears, immunoperoxidase, in-situ hybridization, and vaginal cultures for the presence of cellular herpes simplex and human papillomavirus antigens, nuclei acids, and the existence of cellular atypias which may indicate predisposition to neoplastic transformation at some future date.

PRIOR AND CURRENT PROGRESS

Patient recruitment was completed by Spring 1989. All cytology materials submitted were evaluated by both the Department of Pathology at Walter Reed (Dr. Woodward) and the Department of Cytology at the Armed Forces Institute of Pathology (Dr. Marcella). Standardization of the molecular hybridization techniques with reliable detection of viral DNA could not be accomplished in the laboratory. Attempts to confirm presence of either herpes virus antigen or papillomavirus capsid antigen could not be completed due to an inability to obtain the Bovine papillomavirus capsid antibody. The study was terminated by September 1989.

CONCLUSIONS

A technique to rapidly document the presence or absence of either papillomavirus or herpes simplex virus in exfoliated cells could not be developed such that it would be applicable to widespread laboratory use.

REPORT DATE: 05/14/91

WORK UNIT # 4260

DETAIL SUMMARY SHEET

TITLE: The Utility of Leopold's Maneuvers in Determining Fetal Presentation at 36 Weeks Gestation

KEYWORDS: Leopold's maneuvers, fetal presentation, gestation

PRINCIPAL INVESTIGATOR: Hume, Roderick MAJ MC

ASSOCIATES: Bettencourt, Elizabeth CPT MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the accuracy of Leopold's maneuvers, a traditional series of examinations involving abdominal palpation, in determining fetal presentation at 36 weeks' gestation.

TECHNICAL APPROACH

All obstetric patients at WRAMC are evaluated by Leopold's maneuvers at 36 weeks' gestation. Study participants undergo an ultrasound evaluation to determine the accuracy of the presentation as determined by the maneuvers.

PRIOR AND CURRENT PROGRESS

Extensive data had been obtained on approximately 100 patients. This preliminary data indicated a good correlation between Leopold's maneuvers and ultrasound. However, all the data sheets were lost, making further study impossible.

CONCLUSIONS

Due to lost data, unable to draw final conclusions.

REPORT DATE: 07/01/91

WORK UNIT # 4262

DETAIL SUMMARY SHEET

TITLE: A Multicenter Randomized Trial of Adjuvant Cisplatin/Bleomycin Plus Whole Pelvis Irradiation Vs. Cisplatin/Bleomycin Alone in High Risk Stage IB and IIA Carcinoma of the Cervix

KEYWORDS: carcinoma, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To evaluate the effect of adjunctive pelvic irradiation added to adjunctive chemotherapy for high risk Stage IB and IIA cervical cancer as measured by progression-free interval and survival; and b) To compare the relative toxicities of two regimens with respect to serious complications and/or side effects.

TECHNICAL APPROACH

To be eligible, patients must have had a radical hysterectomy with pelvic and para-aortic lymphadenectomy for Stage IB or IIA cervical carcinoma. They must have one or more of the following poor prognostic signs: nodal metastasis, parametrial involvement, positive surgical margin, tumor diameter greater than 4 cm, deep cervical invasion, adenocarcinoma, adenosquamous carcinoma, or small cell histologic type. Patients are randomized to receive postoperative chemotherapy alone or chemotherapy plus pelvic irradiation.

PRIOR AND CURRENT PROGRESS

To date, 25 patients have been entered into this study. Walter Reed has entered four patients. No significant toxicity has been reported thus far.

CONCLUSIONS

Too early.

REPORT DATE: 08/20/91

WORK UNIT # 4279

DETAIL SUMMARY SHEET

TITLE: Epidermal Growth Factor and Endometrial Growth

KEYWORDS: EGF, endometrium, radioreceptor

PRINCIPAL INVESTIGATOR: Troche, Vladimir MAJ MC

ASSOCIATES: Schaudies, Paul CPT MS

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 908 Previous FYs: \$ 0 Total: \$ 908

STUDY OBJECTIVE

To study the epidermal growth factor (EGF) receptor and its ligand during the normal human menstrual cycle in an attempt to document receptor and ligand alterations in response to the morphologic changes normally seen in the endometrium during the normal menstrual cycle.

TECHNICAL APPROACH

The recruitment of participants and the ligand assay are being performed as presented in the initial protocol. The endometrial membrane preparation for the EGF receptor assay has been modified as follows. The endometrium is homogenized in 5 volumes of ice cold 10 mM Tris-HCL, pH 7.5 containing 25 mM sucrose and 1 mM EDTA in a Dounce homogenizer. The homogenates are centrifuged in a Beckman JA-20 rotor at 3400 rpm at 4C for 10 min. The nuclear pellets are discarded, and the resultant clear supernatants are centrifuged in a Beckman 60Ti rotor at 40,000 rpm at 4C for 60 min. These supernatants are discarded, and the resultant endometrial plasma membrane pellets are resuspended in 0.2% MEM/BSA solution.

PRIOR AND CURRENT PROGRESS

No new subjects have been enrolled into the study in the last year. Total enrollment remains at the same number as the previous report (60). No serious or adverse reactions seen; no subjects withdrawn from the study. Some infertility patients participating in the study benefited from the histologic evaluation performed in the endometrial biopsy.

CONCLUSIONS

The endometrial EGF receptor content is cycle dependent, being maximal during the periovulatory period and minimal just before, during or after menses. This cyclic variation in receptor content may be the result of the physiologic fluctuations in sex steroid hormone levels normally seen during the menstrual cycle. These findings further suggest a role for EGF and its receptor in endometrial proliferation and differentiation.

REPORT DATE: 08/22/91

WORK UNIT # 4280

DETAIL SUMMARY SHEET

TITLE: The Use of Lysis of Adhesions in the Treatment of Chronic Pelvic Pain:
A Prospective Analysis

KEYWORDS: adhesions, pelvic pain

PRINCIPAL INVESTIGATOR: Bettencourt, Elizabeth CPT MC
ASSOCIATES: Armstrong, Alicia MAJ MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To prospectively evaluate the efficacy of lysis of adhesions in treating chronic pelvic pain.

TECHNICAL APPROACH

Patients complete a pain questionnaire preoperatively, then undergo lysis of adhesions. The same questionnaire is completed at 6 weeks and 6 months postoperatively.

PRIOR AND CURRENT PROGRESS

Study was not completed since conclusions were dependent upon patients' completion of mailed questionnaires, and too few of them responded, despite multiple attempts to contact them.

CONCLUSIONS

According to the responses of the patients who did answer the questionnaire, lysis of adhesions did not uniformly improve pelvic pain.

REPORT DATE: 07/30/91

WORK UNIT # 4297

DETAIL SUMMARY SHEET

TITLE: Isolation and Characterization of Cell Subpopulations from the Human Corpus Luteum of the Menstrual Cycle

KEYWORDS: corpus luteum, ovary, human

PRINCIPAL INVESTIGATOR: Klein, Thomas COL MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To characterize and quantify specific cell subpopulations from the human corpus luteum at different times of the menstrual cycle.

TECHNICAL APPROACH

Corpora lutea will be obtained from the ovaries of women undergoing pelvic surgery for indications unrelated to their ovaries. Cell subpopulations will be isolated by methods including centrifugation and flow cytometry. Steroidogenic studies on the isolated subpopulations will be performed by standard methods.

PRIOR AND CURRENT PROGRESS

No patients have been recruited at WRAMC, largely for logistical reasons which are not likely to be resolved in the foreseeable future.

CONCLUSIONS

None.

REPORT DATE: 01/31/91

WORK UNIT # 4113

DETAIL SUMMARY SHEET

TITLE: Cooperative Gynecologic Oncology Group

KEYWORDS: gynecologic, oncology, group

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jan 1974

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Walter Reed section of Gynecologic Oncology is involved with the nationally organized Gynecologic Oncology Group, consisting of 40 major medical centers in the country who are interested in the area of gynecologic tumors and the treatment of gynecologic cancer. The GOG is recognized and funded through the National Cancer Institute.

TECHNICAL APPROACH

Walter Reed is active in approximately 40 GOG protocols. Presently, there are 60 protocols that are either active or continue to provide significant data. These protocols involve treatment of ovarian carcinoma, cervical carcinoma, adenocarcinoma of the endometrium, uterine sarcoma, vulvar carcinoma, and gestational trophoblastic disease.

PRIOR AND CURRENT PROGRESS

Approximately 737 patients have been entered into GOG protocols from Walter Reed. There have been 24 patients entered since the last report.

CONCLUSIONS

Detailed in individual reports.

REPORT DATE: 03/31/91

WORK UNIT # 4160

DETAIL SUMMARY SHEET

TITLE: GOG 40: A Clinical-Pathological Study of Stage I and II Uterine Sarcomas

KEYWORDS: uterus, sarcoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Mar 1979

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of pelvic and aortic lymph node metastasis associated with Stage I and II uterine sarcomas and the relationship of these node metastases to other important prognostic factors, such as mitotic indices of the tumor and complication rate of the procedures.

TECHNICAL APPROACH

All patients with histologically proven uterine sarcoma, clinically Stage I and II, who are medically suited for hysterectomy and lymphadenectomy, are eligible. The patients will undergo, at a minimum, an extrafascial hysterectomy, BSO, and selective pelvic and para-aortic lymphadenectomy. Peritoneal cytology will be obtained. All histologic types of uterine sarcomas are acceptable.

PRIOR AND CURRENT PROGRESS

There are currently 530 patients entered into this protocol from the entire GOG; of whom 447 are evaluable. Walter Reed has entered 14 patients; of whom 14 are evaluable. Among all the patients entered into this study, one had grade 3 hematologic, one had grade 3 GI, and one had grade 4 cutaneous adverse effects; two patients died due to surgical complications. This study has closed to new patient entry but remains open for follow-up data collection.

CONCLUSIONS

The rate of lymphatic node metastasis is low, while the recurrence rate is 4%. Adverse prognostic factors include node metastasis, adnexal involvement, tumor size, myometrial invasion, and lymphatic-vascular space involvement. Histologic grade appears more significant than the mitotic index. The type of heterologous element is not significant. There have been four serious adverse effects, with two postoperative deaths reported.

REPORT DATE: 03/31/91

WORK UNIT # 4163

DETAIL SUMMARY SHEET

TITLE: GOG 26C: A Phase II Trial of Cis-platinum in the Treatment of Advanced Gyn Cancer

KEYWORDS: cis-platinum, diaminedichloroplatinum, gynecologic cancer

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Mar 1979

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of cis-platinum in the treatment of advanced or recurrent gynecologic cancers. A rejection type design will be used involving the fixed sample size of 25 disease patients per disease site per drug or drug use in the study. The design allows replacement of ineffective regimens by newer agents or combinations.

TECHNICAL APPROACH

Cis-platinum appears to exert its cytotoxic action by cross-linking DNA and thus acting in a manner similar to the bifunctional alkylating agents. It has demonstrated activity in animal studies against transitional cell carcinoma in mice. Toxicity in animals reveals myelosuppression, lymphoid atrophy, hemorrhagic enterocolitis, renal tubular necrosis, and cochlear damage, as well as some degree of immunosuppression.

PRIOR AND CURRENT PROGRESS

There have been 563 patients entered into this protocol for the entire GOG; 7 have been entered from Walter Reed. Combinations of cis-platinum and other chemotherapeutic agents are in the process of being tested in other GOG protocols. This protocol is closed to patients with squamous cell carcinoma of the cervix, epithelial carcinoma of the ovary, endometrial adenocarcinoma, non-squamous carcinoma of the uterus, and uterine sarcomas (first line). No grade 4 toxicities have been reported.

CONCLUSIONS

Cis-platinum has marked activity as first-line chemotherapy in squamous cell carcinoma of the cervix, endometrial cancer, and mixed mesodermal sarcomas of the uterus, and is active as second-line therapy for advanced ovarian adenocarcinoma and mixed mesodermal sarcoma of the uterus at the dose and schedule tested. The drug seems to be inactive as first or second line therapy against endometrial and vulvar carcinomas and for leiomyosarcoma of the uterus.

REPORT DATE: 07/01/91

WORK UNIT # 4187

DETAIL SUMMARY SHEET

TITLE: GOG 26N: A Phase II Trial of Dihydroxyanthracenedione (DHAD) in Patients with Advanced Pelvic Malignancies

KEYWORDS: dihydroxyanthracenedione, pelvic malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert COL MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Apr 1981

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of dihydroxyanthracenedione (DHAD) in treating patients with advanced pelvic malignancies.

TECHNICAL APPROACH

Patients with histologically-confirmed advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression are eligible.

PRIOR AND CURRENT PROGRESS

A total of 189 patients have been entered into this protocol. Walter Reed has entered one patient into this study. The protocol is closed to patients with non-squamous carcinoma of the cervix, carcinoma of the vulva/vagina, mixed mesodermal tumors (sarcoma), and leiomyosarcomas. Among all the patients entered into this study, only one has experienced grade 4 hematologic toxicity.

CONCLUSIONS

The data includes minimal activity with DHAD in patients with ovarian cancer who have previously received doxorubicin. In patients with previously treated advanced carcinoma of the cervix, this drug also shows minimal activity. Patients with non-squamous carcinoma of the cervix, endometrium, vulva, vagina, and uterine sarcomas likewise have minimal response to DHAD.

REPORT DATE: 03/19/91

WORK UNIT # 4194

DETAIL SUMMARY SHEET

TITLE: GOG 26-0: A Phase II Trial of Aziridinybenzoquinone (AZQ), in Patients with Advanced Pelvic Malignancies

KEYWORDS: aziridinybenzoquinone, pelvic malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert COL MC

DEPARTMENT: Department of Obstetrics and Gynecology
SERVICE: Gynecologic Oncology Group

STATUS: Completed
APPROVAL DATE: Nov 1981

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of aziridinybenzoquinone (AZQ) in the treatment of advanced pelvic malignancies.

TECHNICAL APPROACH

Patients with histologically confirmed, advanced, recurrent persistent metastatic or local gynecologic cancer with documented disease progression, not amenable to higher priority protocols or standard regimens of therapy, are eligible.

PRIOR AND CURRENT PROGRESS

There have been a total of 183 patients entered into this protocol from the entire GOG. There have been seven patients entered from Walter Reed and its affiliates. The protocol was closed to epithelial ovarian carcinoma in February 1983 and closed to squamous cell carcinoma of the cervix in November 1984. No grade 4 toxicities have been reported.

CONCLUSIONS

AZQ has little, if any, activity as a salvage agent in either epithelial ovarian cancer or squamous cell carcinoma of the cervix and minimal activity in carcinoma of the endometrium and non-squamous cell carcinoma of the cervix.

REPORT DATE: 01/31/91

WORK UNIT # 4203

DETAIL SUMMARY SHEET

TITLE: GOG 26Q: A Phase II Trial of Aminothiadiazole in Patients with
Advanced Pelvic Malignancies

KEYWORDS: aminothiadiazole, pelvic malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jan 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol will constitute a Phase II design to determine the efficacy of aminothiadiazole in treating advanced pelvic malignancies.

TECHNICAL APPROACH

Aminothiadiazole (A-TD) will be administered at a dose of 125 mg/m² IV per week. All patients will continue to receive A-TD until progression of disease is documented or adverse effects prohibit further therapy.

PRIOR AND CURRENT PROGRESS

There have been 135 patients entered into this protocol through the entire GOG. One patient has been entered from Walter Reed. The protocol has been closed to epithelial tumors of the ovary, squamous cell carcinoma of the cervix, non-squamous cell carcinoma of the cervix, and endometrial adenocarcinoma. There have been two grade 4 hematologic toxicities reported.

CONCLUSIONS

Aminothiadiazole used in this dose and schedule has minimal activity in previously treated patients with ovarian carcinoma and squamous cell carcinoma of the cervix, non-squamous cell carcinoma of the cervix and endometrial adenocarcinoma.

REPORT DATE: 07/01/91

WORK UNIT # 4204

DETAIL SUMMARY SHEET

TITLE: GOG 71: Treatment of Patients with Suboptimal Stage IB Carcinoma of the Cervix (Phase III)

KEYWORDS: carcinoma, cervix, hysterectomy

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed

SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate adjunctive extrafascial hysterectomy in the treatment of suboptimal Stage I-B carcinoma of the cervix with negative para-aortic and high common iliac nodes, as well as evaluation of survival and pattern of failure in "bulky" Stage I-B cervical cancer. To evaluate the prognostic value of various surgical/pathological characteristics in suboptimal Stage I-B carcinoma.

TECHNICAL APPROACH

Patients will be randomized after non-invasive evaluation of para-aortic and high common iliac nodes is completed. If nodes are negative, randomization to radiation therapy alone versus radiation therapy plus extrafascial hysterectomy will be performed. If noninvasive evaluation of nodes reveals suspicious positive nodes, fine needle aspiration will be attempted. If needle aspiration is negative, treatment will be given at the discretion of the principal investigator.

PRIOR AND CURRENT PROGRESS

The total number of patients entered into this protocol is 227 for the entire GOG. Walter Reed has entered 10 patients. Nine grade 4 toxicities have been reported from among 175 patients. This protocol was inadvertently submitted twice. This protocol is superseded by Work Unit #4225.

CONCLUSIONS

None.

REPORT DATE: 01/31/91

WORK UNIT # 4208

DETAIL SUMMARY SHEET

TITLE: GOG 73: A Clinicopathologic Study of Primary Malignant Melanoma of the Vulva Treated by Modified Radical Hemivulvectomy

KEYWORDS: melanoma, vulva, hemivulvectomy

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jan 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the relationship of histopathologic parameters (including microstaging of primary malignant melanoma of the vulva) to FIGO staging, and ultimate prognosis. To ultimately recommend appropriate therapy for malignant melanomas of the vulva based on histopathologic and microstaging data.

TECHNICAL APPROACH

All patients receiving primary therapy for primary malignant melanoma of the vulva, including all histopathologic types and differentiation and all FIGO stages, are eligible. All patients must have at least a modified radical hemivulvectomy. All patients must be entered within 8 weeks of initiation of primary therapy.

PRIOR AND CURRENT PROGRESS

A total of 81 patients have been entered into this protocol for the entire GOG, of which 74 have been considered evaluable. Two patients have been entered from Walter Reed. No deaths have been reported resulting from complications of this therapy. This study was closed to patient entry in July 1990.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4212

DETAIL SUMMARY SHEET

TITLE: GOG 72: Ovarian Tumors of Low Malignant Potential: A Study of the Natural History and a Phase II Trial of Melphalan and Secondary Treatment with Cisplatin in Patients with Progressive Disease

KEYWORDS: ovary, malignant, potential

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: May 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The objective of this study is to evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially a Phase II study of melphalan); and to evaluate the response rate to cis-platin in melphalan failures.

TECHNICAL APPROACH

All patients with ovarian tumors considered to have a pathologic classification of low malignancy potential by a study reference pathologist will be eligible. Patients must have undergone adequate surgical staging procedures. Patients may have any stage of disease (from I-IV).

PRIOR AND CURRENT PROGRESS

There have been 351 patients entered into this study; 263 of whom are evaluable. Walter Reed has entered 20 patients into this study. No significant toxicities have been reported among the patients treated.

CONCLUSIONS

Too early.

DETAIL SUMMARY SHEET

TITLE: GOG 26S: A Phase II Trial of Teniposide (VM-26) in Patients with Advanced Pelvic Malignancies

KEYWORDS: teniposide, pelvic, malignancy

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jul 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of teniposide (VM-26) in the treatment of patients with advanced pelvic malignancies.

TECHNICAL APPROACH

Patients with histologically confirmed advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression are eligible for treatment. The treatment consists of VM-26, 100mg/m² IV every week until progression of disease, or the evidence of adverse effects, prohibits further therapy.

PRIOR AND CURRENT PROGRESS

The entire GOG has entered 117 patients into this protocol. Walter Reed has entered no patients. Entry is now closed to patients with ovarian epithelial tumors, squamous cell carcinoma of the cervix, and non-squamous cell carcinoma of the cervix. Two grade 4 toxicities were reported, granulocytopenia.

CONCLUSIONS

Teniposide produced only modest activity in previously treated patients with epithelial ovarian cancer, squamous cell carcinoma of the cervix, non-squamous cell carcinoma of the cervix, or carcinoma of the endometrium.

DETAIL SUMMARY SHEET

TITLE: GOG 71: Treatment of Patients with Suboptimal (Bulky) Stage IB
Carcinoma of the Cervix: A Randomized Comparison of Radiation Therapy
Vs. Radiation Therapy plus Adjuvant Extrafascial Hysterectomy, Phase
III

KEYWORDS: suboptimal, carcinoma, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jul 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Evaluation of the role of adjunctive extrafascial hysterectomy in the treatment of suboptimal Stage I-B carcinoma of the cervix with negative para-aortic and high common iliac nodes. Evaluation of the survival and pattern of failure in suboptimal Stage I-B cancer.

TECHNICAL APPROACH

Patients with untreated, histologically confirmed Stage I-B barrel carcinoma of the cervix will undergo evaluation of para-aortic or high common iliac nodes by CT, lymphangiogram, or sonogram. If the nodes are suspicious or positive, they will be evaluated by surgery or fine needle aspiration. If surgically or cytologically negative or negative by extrinsic evaluation, the patient will be randomized to receive radiation alone or radiation followed by extrafascial hysterectomy.

PRIOR AND CURRENT PROGRESS

To date, 265 patients have been entered into this protocol by the entire GOG. Walter Reed has entered 10 patients. There have been five grade 4 gastrointestinal toxicities. Of the other four grade 4 toxicities, one was urinary, one was neurologic, and two were cardiovascular.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4229

DETAIL SUMMARY SHEET

TITLE: GOG 86A: Master Protocol for Phase II Drug Studies in Treatment of
Advanced or Recurrent Carcinoma of the Endometrium

KEYWORDS: advanced, carcinoma, endometrium

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Apr 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This study seeks to identify additional active agents for treating advanced or recurrent endometrial adenocarcinoma by studying single new drugs in patients with this disease who have not been previously exposed to chemotherapy.

TECHNICAL APPROACH

Patients must have histologically confirmed advanced, persistent, or recurrent endometrial carcinoma with documented disease progression after local therapy. All patients must have measurable disease. Patients must have failed local therapeutic measures or must be considered incurable with local therapy.

PRIOR AND CURRENT PROGRESS

GOG 86A is a master protocol. Please see individual protocols.

CONCLUSIONS

See individual protocols.

REPORT DATE: 07/01/91

WORK UNIT # 4231

DETAIL SUMMARY SHEET

TITLE: GOG 87A: Master Protocol for Phase II Drug Studies in the Treatment of Recurrent or Advanced Uterine Sarcomas

KEYWORDS: advanced, uterus, sarcoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: May 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To allow the best possible chance for a new cytotoxic agent to demonstrate activity, this study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The study design will involve treating an average sample size of 30 patients per drug studied for each of the following cell categories: mixed mesodermal tumor, leiomyosarcoma, and other sarcomas.

TECHNICAL APPROACH

Patients will have histologically confirmed advanced, persistent, or recurrent uterine sarcoma with documented disease progression after appropriate local therapy. Each patient will receive a chemotherapeutic regimen as outlined in each segment of the protocol.

PRIOR AND CURRENT PROGRESS

There have been 86 patients entered into the GOG 87B section of this protocol; 5 patients have been entered into this study from Walter Reed. Of all the patients entered into GOG 87B, eight experienced grade 4 leukopenia, one grade 4 thrombocytopenia, six grade 4 granulocytopenia, and two grade 4 neurotoxic effects. There has been one death reported believed related to the therapy. GOG 87-B was closed for mixed mesodermal tumors in March 1988. There have been 71 patients entered into GOG 87C; one patient has been entered from WRAMC. One patient had a grade 4 leukopenia.

CONCLUSIONS

See individual protocols.

REPORT DATE: 07/01/91

WORK UNIT # 4232

DETAIL SUMMARY SHEET

TITLE: GOG 87B: A Phase II Trial of Ifosfamide and the Uroprotector, Mesna, in the Treatment of Recurrent or Advanced Uterine Sarcomas

KEYWORDS: ifosfamide, Mesna, sarcoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: May 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This study is designed to allow the best possible chance for a new cytotoxic agent to demonstrate activity, constituting a Phase II design in a population of patients who have had no prior drug therapy. The study design will involve treating an average sample size of 30 evaluable patients with ifosfamide for each of the following cell type categories: mixed mesodermal tumor, leiomyosarcoma, and other sarcomas.

TECHNICAL APPROACH

Patients will have histologically confirmed advanced, persistent, or recurrent uterine sarcoma with documented disease progression after appropriate local therapy. Each patient will receive ifosfamide and mesna for five days every 4 weeks until disease progression or adverse effects prohibit further therapy.

PRIOR AND CURRENT PROGRESS

There have been 86 patients entered into this protocol for the entire GOG; 73 of whom are evaluable. Walter Reed has entered five patients into this study. Of all the patients treated on protocol 87B, eight experienced grade 4 leukopenia, one experienced grade 4 thrombocytopenia, six experienced grade 4 granulocytopenia, and two experienced neurotoxic effects.

CONCLUSIONS

Ifosfamide/mesna may be the most active single agent therapy for advanced mixed mesodermal tumors of the uterus.

REPORT DATE: 08/29/91

WORK UNIT # 4234

DETAIL SUMMARY SHEET

TITLE: GOG 26U: A Phase II Trial of Ifosfamide and the Uroprotector, Mesna, in Patients with Advanced Pelvic Malignancies

KEYWORDS: ifosfamide, Mesna, malignancy

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Aug 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The objective of this study is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to higher priority methods of treatment. A "rejection"-type design will be used involving a fixed sample size of 25 patients per disease site per drug or combination of drugs studied.

TECHNICAL APPROACH

Ifosfamide, like cyclophosphamide, requires activation by a hepatic microsomal NADPH-dependent mixed-function oxidase system. A bi-ability to crosslink and fragment DNA is produced. Mesna has been shown to acceptably reduce the urothelial toxicity of ifosfamide in several European studies. All patients must have biopsy proven advanced pelvic malignancy to be eligible.

PRIOR AND CURRENT PROGRESS

The entire GOG has entered 194 patients into this study. Walter Reed has entered five patients. There have been eight grade 4 toxicities for ovarian sarcoma: leukopenia three, granulocytopenia four, and renal one. For non-squamous cell carcinoma there have been nine grade 4 toxicities: thrombocytopenia one, granulocytopenia six, GU one, and alopecia one.

CONCLUSIONS

Ifosfamide is an active Phase II drug in relapsed epithelial ovarian carcinoma, although nephro-toxicity is a limiting factor in this patient population. Ifosfamide possesses minimal activity in previously treated squamous carcinoma of the cervix.

REPORT DATE: 10/31/91

WORK UNIT # 4235

DETAIL SUMMARY SHEET

TITLE: GOG 83: A Clinico-Pathologic Study of Simultaneous Endometrial and Ovarian Carcinomas

KEYWORDS: endometrial, ovarian, carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Sep 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine the natural history of patients with synchronous adenocarcinoma presenting in both the endometrium and the ovary, and to obtain estimates of mortality at five years. b) To determine whether histologic criteria or pattern of spread can be used to distinguish subsets of patients with differing prognoses.

TECHNICAL APPROACH

Simultaneous endometrial and ovarian carcinomas are defined for the purpose of this protocol as cancers occurring in those two sites which have been diagnosed within 8 weeks of each other. To be eligible, patients must have undergone surgical and pathological procedures outlined in the protocol, after which they will be followed to determine the natural history of this disease process.

PRIOR AND CURRENT PROGRESS

Thus far, 80 patients have been entered into this study by the entire GOG. Walter Reed has entered one patient. No toxicity has been reported. This protocol was closed to patient entry in July 1991. Follow-up is required for the one patient entered.

CONCLUSIONS

Too early for analysis.

REPORT DATE: 11/30/90

WORK UNIT # 4239

DETAIL SUMMARY SHEET

TITLE: GOG 85: A Randomized Comparison of Hydroxyurea Vs. 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy in Patients with Stage IIB, III, and IVA Carcinoma of the Cervix

KEYWORDS: chemotherapy, carcinoma, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert COL MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Nov 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine whether hydroxyurea or the combination of 5-fluorouracil and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma; and b) To determine the relative toxicities of hydroxyurea versus the combination of 5-fluorouracil and cisplatin when given with radiation therapy.

TECHNICAL APPROACH

Eligible patients include those with primary, previously untreated, histologically confirmed, invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma of the uterine cervix (Stages II-B, III-A, III-B, and IV-A), with negative para-aortic nodes. Patients who have had para-aortic lymphadenectomy and intraperitoneal exploration with cytologic washings, as outlined in the protocol, are also included.

PRIOR AND CURRENT PROGRESS

To date, 388 patients have been entered into this study. Twenty patients have been entered from Walter Reed. Eleven patients have experienced a grade 4 hematologic toxicity. No patients have died from treatment toxicity. This study was closed to patient entry as of November 1990.

CONCLUSIONS

Too early.

REPORT DATE: 03/31/91

WORK UNIT # 4244

DETAIL SUMMARY SHEET

TITLE: GOG 90: Evaluation of Cisplatin, Etoposide and Bleomycin (BEP)
Induction Followed by Vincristine, Dactinomycin and Cyclophosphamide
(VAC) Consolidation in Advanced Ovarian Germ Cell Tumors, Phase II

KEYWORDS: ovarian, germ cell, tumors

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Mar 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP), followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors.

TECHNICAL APPROACH

Eligible patients include those with histologically confirmed malignant germ cell tumors of the ovary who have incompletely resected Stage II, III, or IV disease. Patients who have previously received pelvic radiation therapy will be eligible, but the initial dose of etoposide will be reduced 20%.

PRIOR AND CURRENT PROGRESS

To date, 54 patients have been entered into this protocol by all GOG member institutions. No patient has been entered from Walter Reed. There have been 24 episodes of grade 4 granulocytopenia, two episodes of grade 4 thrombocytopenia, one grade 4 gastrointestinal reaction, and one grade 4 allergic reaction.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4245

DETAIL SUMMARY SHEET

TITLE: GOG 97: A Phase III Randomized Study of Cyclophosphamide and Cisplatin in Patients with Suboptimal Stage III and IV Epithelial Ovarian Carcinoma Comparing Intensive and Non-Intensive Schedules

KEYWORDS: epithelium, ovarian, carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert COL MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Completed

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol seeks to determine response rate, response duration, and survival in suboptimal Stage III and Stage IV ovarian carcinoma treated with cyclophosphamide and cisplatin, administered by two different schedules, one intense and the other standard.

TECHNICAL APPROACH

Eligible patients include those with established ovarian epithelial cancer, suboptimal (more than 1 cm in diameter) Stages III and IV. All patients must have optimal surgery ovarian carcinoma, with an exploratory laparotomy and appropriate tissue for histologic evaluation.

PRIOR AND CURRENT PROGRESS

There have been 485 patients entered into this study for the entire GOG; 424 of whom are evaluable. Walter Reed has entered 11 patients into this study. Of all the patients entered into this study, 103 experienced grade 4 hematologic adverse effects, four experienced grade 4 GI adverse effects, and five experienced grade 4 renal adverse effects. This protocol was closed to new patient entry in April 1990.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4246

DETAIL SUMMARY SHEET

TITLE: GOG 94: A Phase II Study of the Treatment of Papillary Serous
Carcinoma of the Endometrium Stage I and II and Maximally Debulked
Advanced Endometrial Carcinoma with Total Abdominal Radiation Therapy

KEYWORDS: papillary, carcinoma, endometrium

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert COL MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol is designed to determine the survival and progression-free interval of patients with maximally debulked advanced endometrial carcinoma treated with abdominal radiation therapy.

TECHNICAL APPROACH

All patients with primary endometrial carcinoma, clinical and surgical Stages III and IV disease (all histologic types), all clinical and surgical stages of clear cell carcinoma, and all clinical and surgical stages of papillary serous carcinoma are eligible. Tumor must be maximally debulked at 2 cm or less.

PRIOR AND CURRENT PROGRESS

There have been 202 patients entered into this study from the entire GOG; Walter Reed has entered six patients. Two grade 4 GI toxicities have been reported among the 154 patients.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4247

DETAIL SUMMARY SHEET

TITLE: GOG 95: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C) and Selected Stage IAI and IBI and IAIi and IBIi Ovarian Cancer, Phase III

KEYWORDS: randomized, ovarian, cancer

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert COL MC

DEPARTMENT: Department of Obstetrics and Gynecology
SERVICE: Gynecologic Oncology Group

STATUS: Ongoing
APPROVAL DATE: May 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This study seeks to compare the progression-free interval and overall survival between P32 and a combination of cyclophosphamide and cisplatin for patients with early ovarian cancer and to determine the patterns of relapse for each form of therapy.

TECHNICAL APPROACH

All patients must have a histopathologic diagnosis of epithelial ovarian cancer of each histologic cell type: serous mucinous; others include endometrioid, transitional mesonephroid (clear cell), adenocarcinoma (endometrioid with squamous metaplasia), mixed epithelial, unclassifiable (undifferentiated).

PRIOR AND CURRENT PROGRESS

There have been 112 patients entered into this study from the entire GOG; Walter Reed has entered six patients. Ten patients have developed grade 4 leukopenia.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4250

DETAIL SUMMARY SHEET

TITLE: GOG 88: A Randomized Study of Radical Vulvectomy and Bilateral Groin Dissection Vs. Radical Vulvectomy and Bilateral Groin Radiation, Phase III

KEYWORDS: radical, vulvectomy, radiation

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To evaluate the comparative efficacy and morbidity of groin radiation therapy in lieu of groin dissection for selected patients with invasive squamous cell carcinoma of the vulva; and b) To monitor patterns of recurrence and survival of patients treated with groin radiation therapy in lieu of groin dissection.

TECHNICAL APPROACH

Eligible patients include those with primary, previously untreated, histologically confirmed, invasive squamous cell carcinoma of the vulva which has been clinically determined to be Stage I through III and which radical vulvectomy would suffice to remove all of the primary lesion.

PRIOR AND CURRENT PROGRESS

To date, the entire GOG has entered 52 patients into this protocol. Walter Reed has entered no patients into this protocol. This protocol was closed in November 1990.

CONCLUSIONS

Too early.

REPORT DATE: 07/31/91

WORK UNIT # 4251

DETAIL SUMMARY SHEET

TITLE: GOG 26W: A Phase II Trial of Echinomycin in Patients with Advanced Pelvic Malignancies

KEYWORDS: echinomycin, pelvic malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of echinomycin in the treatment of advanced or recurrent pelvic malignancies.

TECHNICAL APPROACH

Eligible patients include those who have histologically confirmed recurrent or metastatic gynecologic cancer which is refractory to curative therapy or established treatments. All patients must have measurable disease.

PRIOR AND CURRENT PROGRESS

The entire GOG has entered 86 patients into this study to date. Walter Reed has entered four patients. One grade 4 thrombocytopenia has been reported. This study has been closed to patients with epithelial ovarian carcinoma or squamous cell carcinoma but remains open to patients with other types of gynecologic malignancy.

CONCLUSIONS

Echinomycin displays minimal activity in patients with squamous cell carcinoma of the cervix and ovarian epithelial carcinoma who have had prior chemotherapy.

REPORT DATE: 10/31/91

WORK UNIT # 4253

DETAIL SUMMARY SHEET

TITLE: GOG 81F: A Phase II Trial of Tamoxifen Citrate in Patients with
Advanced or Recurrent Endometrial Carcinoma Responsive to Progestins

KEYWORDS: tamoxifen, endometrial, carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether patients with endometrial carcinoma who have responded to medroxyprogesterone acetate and then progressed will respond to a second hormonal manipulation in the form of tamoxifen citrate.

TECHNICAL APPROACH

To be eligible, patients must have histologically confirmed advanced, persistent, or recurrent endometrial carcinoma with documented disease progression after local therapy. Patients must have measurable disease. Patients must have been treated with medroxyprogesterone acetate and have been partial responders.

PRIOR AND CURRENT PROGRESS

The entire GOG has entered 82 patients into this study to date. Walter Reed has entered no patients. No grade 4 toxicities have been reported.

CONCLUSIONS

Too early.

REPORT DATE: 08/29/91

WORK UNIT # 4254

DETAIL SUMMARY SHEET

TITLE: GOG 93: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma, Stage III, Phase III

KEYWORDS: chromic phosphate, ovarian, carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the role of intraperitoneal chromic phosphate suspension therapy in patients with Stage III epithelial ovarian carcinoma who have no detectable evidence of disease at the second-look laparotomy.

TECHNICAL APPROACH

To be eligible, patients must have histologically confirmed primary epithelial carcinoma of the ovary and be in complete clinical remission. Patients must have a diagnosis of FIGO Stage III ovarian carcinoma.

PRIOR AND CURRENT PROGRESS

The entire GOG has entered 63 patients into this study. Walter Reed has entered no patients. No grade 4 toxicities have been reported.

CONCLUSIONS

Too early.

REPORT DATE: 10/01/91

WORK UNIT # 4255

DETAIL SUMMARY SHEET

TITLE: GOG 78: Evaluation of Adjuvant Vinblastine, Bleomycin and Cisplatin Therapy in Totally Reducing Choriocarcinoma, Endodermal Sinus Tumor or Embryonal Carcinoma of the Ovary, Pure and Mixed with Other Elements, Phase II

KEYWORDS: VP-16, bleomycin, cisplatin

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Bosscher, James LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology
SERVICE: Gynecologic Oncology Group

STATUS: Ongoing
APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effect of adjuvant VP-16, bleomycin, and cisplatin chemotherapy in patients with endodermal sinus tumor, choriocarcinoma, embryonal carcinoma, and grade 2 and 3 immature teratoma of the ovary after removal of all gross tumors.

TECHNICAL APPROACH

Eligible patients include those with histologically confirmed Stage I choriocarcinoma, endodermal sinus tumor, embryonal carcinoma, and grade 2 and 3 immature teratoma. Patients with Stage II and III disease are also eligible if all gross tumor is removed. Serum AFP and beta-HCG levels should be normal.

PRIOR AND CURRENT PROGRESS

To date, 102 patients have been entered into this study from the entire GOG. Walter Reed has entered one patient. Six patients have had grade 4 leukopenia. One patient had a grade 4 GI toxicity, one patient had a grade 4 dermatologic toxicity, three patients had a grade 4 thrombocytopenia, and 27 patients had a grade 4 granulocytopenia.

CONCLUSIONS

Too early for analysis.

REPORT DATE: 10/31/91

WORK UNIT # 4256

DETAIL SUMMARY SHEET

TITLE: GOG 86E: A Phase II Trial of Vincristine Given as a Weekly Intravenous Bolus in Advanced or Recurrent Endometrial Carcinoma

KEYWORDS: vincristine, endometrial, carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol seeks to determine whether endometrial carcinoma which is refractory to progestogens or which is progressing after initial response to progestogens will respond to vincristine.

TECHNICAL APPROACH

Patients must have histologically confirmed advanced, persistent, or recurrent endometrial carcinoma with documented disease progression after local therapy. All patients must have measurable disease. It is required that patients have received no prior chemotherapy.

PRIOR AND CURRENT PROGRESS

To date, 36 patients have been entered into this study by the entire GOG. Walter Reed has entered one patient. No grade 4 toxicities have been reported. Grade 3 neurologic toxicity has been reported in three patients. This study is now closed to new patient entry. The one patient entered by Walter Reed has been taken off this protocol and entered on another; therefore, no follow-up is required on this protocol.

CONCLUSIONS

Vincristine displays moderate activity in endometrial cancer. There is no significant toxicity.

REPORT DATE: 10/31/91

WORK UNIT # 4257

DETAIL SUMMARY SHEET

TITLE: GOG 99: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

KEYWORDS: radiation, endometrial, adenocarcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to their lymph nodes benefit from postoperative pelvic radiotherapy. To evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

TECHNICAL APPROACH

Patients with primary histologically confirmed grades 2 and 3 endometrial adenocarcinoma are eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node sampling, pelvic washings, and found to be surgical Stage I. Patients must have myometrial invasion.

PRIOR AND CURRENT PROGRESS

One hundred and fifty-two patients have been entered into this protocol through the entire GOG. Walter Reed has entered six patients. No grade 4 toxicity has been reported.

CONCLUSIONS

Too early.

REPORT DATE: 08/07/91

WORK UNIT # 4263

DETAIL SUMMARY SHEET

TITLE: GOG 26X: A Phase II Trial of Gallium Nitrate in Patients with Advanced Pelvic Malignancies

KEYWORDS: gallium nitrate, pelvic malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MC

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jun 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of gallium nitrate in the treatment of advanced or recurrent gynecologic cancers.

TECHNICAL APPROACH

Patients will have histologically confirmed recurrent or metastatic gynecologic cancer which is refractory to curative therapy of established treatments.

PRIOR AND CURRENT PROGRESS

To date, 38 patients have been entered into this protocol from the entire GOG. No patients have been entered from Walter Reed. One grade 4 anemia has been reported. This study has been closed to patients with epithelial ovarian carcinoma but remains open to patients with other gynecologic malignancies.

CONCLUSIONS

Gallium nitrate has modest activity in previously treated patients with epithelial ovarian carcinoma.

REPORT DATE: 08/07/91

WORK UNIT # 4264

DETAIL SUMMARY SHEET

TITLE: GOG 26Y: A Phase II Trial of Vinblastine in Patients with Advanced
Pelvic Malignancies

KEYWORDS: vinblastine, advanced, pelvic malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of vinblastine in the treatment of advanced or recurrent gynecologic cancers.

TECHNICAL APPROACH

Patients with histologically confirmed gynecologic cancer, either recurrent or advanced in initial presentation, are eligible.

PRIOR AND CURRENT PROGRESS

To date, 58 patients have been entered into this protocol from the entire GOG. Walter Reed has entered two patients; both of whom have expired. Protocol was closed and terminated in November 1990.

CONCLUSIONS

Vinblastine at the dose and schedule tested is inactive in advanced epithelial ovarian cancer and squamous cell carcinoma of the cervix.

REPORT DATE: 07/25/91

WORK UNIT # 4265

DETAIL SUMMARY SHEET

TITLE: GOG 102 A-B (Master Protocol): Intraperitoneal Administration of
Cisplatin and 5-FU in Residual Ovarian Carcinoma, Phase II

KEYWORDS: cisplatin, 5-fluorouracil, ovarian carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Bosscher, James LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 238 Total: \$ 238

STUDY OBJECTIVE

To determine the activity of cisplatin and 5-fluorouracil when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy.

TECHNICAL APPROACH

Patients with primary, histologically documented, epithelial carcinoma of the ovary. Patients who have had partial or incomplete responses to combination chemotherapy and who have documented minimal residual disease (1.0 cm or less maximum tumor diameter) at second look laparotomy following chemotherapy. Patients with a history of complete response followed by a recurrence with no residual nodule greater than 1 cm in diameter are also eligible.

PRIOR AND CURRENT PROGRESS

There have been 48 patients entered into this protocol for the entire GOG. No patients have been entered from Walter Reed. There has been one grade 4 leukopenia, four grade 4 neutropenias, one grade 4 anemia, and one grade 4 hepatic toxicity. GOG 102B was closed to new patient entry in December 1988; however, the Master Protocol 102A remains in effect. The title of this protocol should be amended to GOG 102A.

CONCLUSIONS

This is an active salvage regimen in small volume cisplatin-sensitive tumors.

REPORT DATE: 08/29/91

WORK UNIT # 4266

DETAIL SUMMARY SHEET

TITLE: GOG 76A: Master Protocol for Phase II Drug Studies in the Treatment of Advanced or Recurrent Squamous Cell Carcinoma of the Cervix.

KEYWORDS: advanced, squamous cell carcinoma, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Continued identification of new active drugs in the treatment of advanced or recurrent squamous cell carcinomas of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

TECHNICAL APPROACH

Patients enrolled in individual protocol under this Master Protocol will have histologically confirmed advanced, persistent, or recurrent squamous cell carcinoma of the cervix with documented disease progression after local therapy.

PRIOR AND CURRENT PROGRESS

GOG 76A is a Master Protocol. Currently at Walter Reed, Protocols 76I and 76S are the only ones in the 76 series that have been approved. Three patients have been entered into Protocol 76I at WRAMC. Approximately 409 patients have been entered into the entire series. There have been a total of 40 grade 4 toxicities: 21 leukopenias, 10 neutropenias, 1 cutaneous, 2 neurotoxicities, 1 fever, 4 thrombocytopenias, and 1 hypocalcemia.

CONCLUSIONS

See individual protocols.

REPORT DATE: 08/28/91

WORK UNIT # 4267

DETAIL SUMMARY SHEET

TITLE: GOG 76I: A Phase II Trial of Ifosfamide and the Uroprotector, Mesna, in Patients with Advanced Squamous Cell Carcinoma of the Cervix

KEYWORDS: ifosfamide, Mesna, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The objective of the study is to continue identification of new active drugs in the treatment of advanced or recurrent squamous cell carcinomas of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

TECHNICAL APPROACH

Patients with histologically confirmed advanced, persistent, or recurrent squamous cell carcinoma of the cervix with documented disease progression after local therapy are accepted into the study. Patients must have bilirubin, SGOT, and liver alkaline phosphatase less than or equal to two times normal.

PRIOR AND CURRENT PROGRESS

The entire GOG has entered 56 patients into this study. Walter Reed has entered three patients. There have been 19 grade 4 toxicities: eleven leukopenia, two neurotoxicities, four neutropenia, one cutaneous, and one fever. This study is closed to patient entry, but we are following patients that are currently on this protocol.

CONCLUSIONS

There appears to be modest activity in this group of patients.

REPORT DATE: 11/30/90

WORK UNIT # 4268

DETAIL SUMMARY SHEET

TITLE: GOG 26DD: A Phase II Trial of Amonafide in Patients with Advanced Pelvic Malignancies

KEYWORDS: amonafide, pelvic, malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of amonafide in the treatment of advanced pelvic malignancies.

TECHNICAL APPROACH

Eligible patients must have histologically confirmed recurrent or metastatic gynecologic cancer which is refractory to curative therapy or established treatments. All patients must have measurable disease.

PRIOR AND CURRENT PROGRESS

To date, 48 patients have been entered into this study by the entire GOG. Walter Reed has entered three patients. There have been 10 grade 4 hematologic toxicities, one grade 4 GI toxicity, and one grade 4 renal toxicity reported. No treatment deaths have been reported.

CONCLUSIONS

Too early.

REPORT DATE: 12/31/90

WORK UNIT # 4272

DETAIL SUMMARY SHEET

TITLE: GOG 87C: A Phase II Trial of Hydroxyurea, Dacarbazine, and Etoposide
in Patients with Advanced or Recurrent Uterine Sarcomas

KEYWORDS: hydroxyurea, dacarbazine, etoposide

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To allow the best possible chance for a new cytotoxic agent to demonstrate activity, this study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The study design will involve treating 30 patients per each drug studied for each of the following cell types: mixed mesodermal tumor, leiomyosarcoma, and other sarcomas.

TECHNICAL APPROACH

Eligible patients must have histologically confirmed advanced, persistent, or recurrent uterine sarcoma with documented disease progression after appropriate local therapy. Histologic types to be included in this study include leiomyosarcoma, mixed mesodermal tumor, endometrial stromal sarcoma, and other uterine sarcomas. All patients must have measurable disease and must be considered incurable.

PRIOR AND CURRENT PROGRESS

To date, 71 patients have been entered into this study by the entire GOG. One patient has been accrued by Walter Reed. Two grade 4 hematologic toxicities and one grade 4 dermatologic toxicity have been reported. There have been no treatment deaths reported.

CONCLUSIONS

Too early.

REPORT DATE: 01/31/91

WORK UNIT # 4274

DETAIL SUMMARY SHEET

TITLE: GOG 104: Intraperitoneal Cisplatinum/Intravenous Cyclophosphamide Vs.
Intravenous Cisplatinum/Intravenous Cyclophosphamide in Patients with
Nonmeasurable Disease Stage III Ovarian Cancer, Phase III

KEYWORDS: cis-platinum, cyclophosphamide, ovary

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To carry out a Phase III randomized trial of intermediate dose intraperitoneal cis-platinum plus intravenous cyclophosphamide versus intermediate dose intravenous cis-platinum plus intravenous cyclophosphamide for optimal Stage III ovarian cancer.

TECHNICAL APPROACH

Patients will be randomized to receive one of the two regimens listed above. Eligible patients must have a histologically confirmed pure epithelial ovarian carcinoma. Those with a borderline tumor will be excluded.

PRIOR AND CURRENT PROGRESS

To date, the entire GOG has accrued 173 patients. Four patients have been entered from Walter Reed. There have been 26 cases of grade 4 neutropenia reported. There have been no treatment related deaths.

CONCLUSIONS

Too early.

REPORT DATE: 03/31/91

WORK UNIT # 4275

DETAIL SUMMARY SHEET

TITLE: GOG 107 A Randomized Study of Doxorubicin Vs. Doxorubicin Plus
Cisplatin in Patients with Primary Stage III and IV Recurrent
Endometrial Adenocarcinoma, Phase III

KEYWORDS: doxorubicin, cisplatin, endometrial

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Mar 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The major objective of this study is to determine whether the addition of cisplatin to doxorubicin offers significant improvement in the frequency of objective response, the duration of progression free interval, and the length of survival as compared to doxorubicin alone.

TECHNICAL APPROACH

Eligible patients must have Stage III, Stage IV, or recurrent endometrial carcinoma. Patients must have measurable disease. Patients may have received prior hormonal therapy or therapy with biologic response modifiers.

PRIOR AND CURRENT PROGRESS

To date, 100 patients have been enrolled by the entire GOG. No patients have been entered from Walter Reed. No significant toxicity has been reported.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4277

DETAIL SUMMARY SHEET

TITLE: GOG 108: Ifosfamide and the Uroprotector, Mesna, with or without
Cisplatin in Patients with Advanced or Recurrent Mixed Mesodermal
Tumors of the Uterus, Phase III

KEYWORDS: ifosfamide, uterine, sarcoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To confirm reported high response rates of advanced or recurrent mixed mesodermal tumors of the uterus to ifosfamide mesna. To determine whether the addition of cis-platin to ifosfamide mesna improves response rates or survival in patients with these tumors.

TECHNICAL APPROACH

Eligible patients include those with primary, histologically confirmed, heterologous or homologous (carcinosarcoma) mixed mesodermal tumors of the uterus. All patients must have measurable disease. Patients who have received prior chemotherapy are not eligible.

PRIOR AND CURRENT PROGRESS

There have been 43 patients entered into this study from the entire GOG. Walter Reed has entered no patients. No toxicity has been reported.

CONCLUSIONS

Too early.

REPORT DATE: 08/29/91

WORK UNIT # 4278

DETAIL SUMMARY SHEET

TITLE: GOG 26EE A Phase II Trial of Didemnin B in Patients with Advanced Pelvic Malignancies

KEYWORDS: Didemnin B, pelvic, malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The objective of this study is to determine the efficacy of Didemnin B in the treatment of advanced or recurrent pelvic carcinomas.

TECHNICAL APPROACH

Eligible patients must have histologically confirmed recurrent or metastatic gynecologic cancer which is refractory to curative therapy or established treatments. All patients must have measurable disease.

PRIOR AND CURRENT PROGRESS

To date, 43 patients have been entered into this study by the entire GOG. Walter Reed has entered no patients. One grade 5 gastrointestinal toxicity has been reported. The protocol is closed to patients with squamous cell cancer of the cervix and epithelial adenocarcinoma of the ovary.

CONCLUSIONS

Didemnin B was ineffective with the schedules utilized for squamous cell cancer of the cervix and epithelial adenocarcinoma of the ovary. It is closed for these gynecologic malignancies but remains open for the remaining gynecologic cancers until adequate accrual is reached and activity can be assessed.

REPORT DATE: 01/31/91

WORK UNIT # 4281

DETAIL SUMMARY SHEET

TITLE: GOG 8801 A Phase I Evaluation of Multiple Daily Fraction Radiation and Hydroxyurea in Patients with Stage IIB, III and IVA Carcinoma of the Cervix with Negative Para-aortic Nodes

KEYWORDS: radiation, hydroxyurea, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the toxicity of accelerated hyperfractionated radiation plus hydroxyurea in patients with cancer of the cervix. To determine the optimal tolerated dose of hyperfractionated radiation when combined with hydroxyurea and intracavitary radiation.

TECHNICAL APPROACH

Patients must have primary previously untreated histologically confirmed carcinoma of the cervix. Squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma are eligible. Patients must have FIGO Stage IIB, IIIA, IIIB, or IV disease with negative para-aortic nodes. Patients must have a para-aortic lymphadenectomy and intraperitoneal exploration with cytologic washings as outlined in the protocol.

PRIOR AND CURRENT PROGRESS

To date, 17 patients have been accrued by the entire GOG. Walter Reed has entered four patients. No toxicity reports are available at this time.

CONCLUSIONS

Too early.

REPORT DATE: 01/31/91

WORK UNIT # 4282

DETAIL SUMMARY SHEET

TITLE: GOG 8901 A Phase I Evaluation of Multiple Daily Fraction Radiation and 5FU Plus Cisplatin in Stage IIB, III and IVA Carcinoma of the Cervix with Negative Para-aortic Nodes

KEYWORDS: radiation, 5-Fu, cisplatin

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology
SERVICE: Gynecologic Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the toxicity of accelerated hyperfractionated radiation plus 5-Fluorouracil (5-FU) and cisplatin in patients with cancer of the cervix. To determine the optimal tolerated dose of hyperfractionated radiation when combined with 5-FU, cisplatin, and intracavitary radiation.

TECHNICAL APPROACH

Patients must have primary previously untreated histologically confirmed carcinoma of the cervix. Squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma are eligible. Patients must have FIGO Stage IIB, IIIB, IVA disease with negative para-aortic nodes. Patients must have a para-aortic lymphadenectomy and intraperitoneal exploration with cytologic washings as outlined in the protocol.

PRIOR AND CURRENT PROGRESS

To date, 13 patients have been accrued by the entire GOG. Walter Reed has entered two patients. No toxicity reports are available at this time.

CONCLUSIONS

Too early.

REPORT DATE: 08/31/91

WORK UNIT # 4283

DETAIL SUMMARY SHEET

TITLE: GOG 33 A Clinical Pathologic Study of Stage I and II Carcinoma of the Endometrium

KEYWORDS: carcinoma, endometrium

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of pelvic and aortic lymph node metastases and the relationship of these node metastases to other prognostic factors in Stage I and II carcinoma of the endometrium.

TECHNICAL APPROACH

Patients enrolled will have a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, and peritoneal cytology sampling. Thereafter, the patient will be followed up or entered onto an additional GOG protocol.

PRIOR AND CURRENT PROGRESS

Protocol was closed to patient entry in July 1982. It was reopened in April 1990 for patient follow-up only of two patients. These two patients are not lost to follow-up; therefore, this protocol is completed.

CONCLUSIONS

Preliminary evaluation would tend to indicate that this larger study verifies the findings of the pilot study. There is increased depth of invasion with increasing grade, and with the increase in grade there is increased involvement of pelvic and aortic nodes. It would appear that this study could define the surgical procedure required for optimal evaluation of endometrial cancer.

REPORT DATE: 08/31/91

WORK UNIT # 4284

DETAIL SUMMARY SHEET

TITLE: GOG 34 A Randomized Study of Adriamycin as an Adjuvant After Surgery and Radiation Therapy in Patients with High Risk Endometrial Carcinoma

KEYWORDS: Adriamycin, endometrium, carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study differences in morbidity and patient survival as functions of various tumor growth patterns as well as treatments.

TECHNICAL APPROACH

All patients with primary, previously untreated, histologically confirmed invasive carcinoma of the endometrium, Stage I and Stage II occult, all grades, with one or more of the high risk criteria: all lesions with equal to or greater than 1/2 myometrial involvement, positive pelvic and/or para-aortic nodes, microscopic evidence of cervical involvement but no gross clinical involvement of the cervix, adnexal metastases.

PRIOR AND CURRENT PROGRESS

There were 224 patients entered from the entire GOG. WRAMC entered nine. This protocol was closed to patient entry in July 1986. Request was made to reopen the protocol in April 1990 for purpose of follow-up only. Protocol was terminated by GOG in April 1990. Therefore, no follow-up is required any longer.

CONCLUSIONS

Very poor accrual made it impossible to achieve the principal goal of this study within an acceptable period of time.

REPORT DATE: 08/01/91

WORK UNIT # 4285

DETAIL SUMMARY SHEET

TITLE: GOG 36 Surgical Pathologic Study of Women with Squamous Cell Carcinoma of the Vulva

KEYWORDS: FIGO, carcinoma, squamous cell

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the validity of current FIGO staging to the pathologic prognosis factors of size of lesion, location of lesion, depth of invasion of tumor in mm, histologic grade, site, and number of positive lymph nodes in Stage I-IV carcinoma of the vulva. To rapidly accumulate prospective surgical-pathological data for development of further protocols. To determine the morbidity of primary radical surgery for vulvar carcinoma.

TECHNICAL APPROACH

All patients with primary, previously untreated, histologically confirmed invasive squamous cell carcinoma of the vulva, determined to be Stage I-IV where radical vulvectomy sufficient to remove all lesions, are eligible. Patients will have radical vulvectomy plus bilateral groin node dissection and will be randomized to follow-up alone (negative groin nodes) or to more advanced protocols involving radiotherapy (positive groin nodes).

PRIOR AND CURRENT PROGRESS

There have been 630 entries into this protocol. This protocol was originally closed in 1986 and reopened in April 1990 for follow-up of two patients only. This protocol was terminated in November 1990.

CONCLUSIONS

Too early.

REPORT DATE: 04/30/91

WORK UNIT # 4286

DETAIL SUMMARY SHEET

TITLE: GOG 44 Evaluation of Adjuvant Vincristine, Dactinomycin and
Cyclophosphamide Therapy in Malignant Germ Cell Tumors of the Ovary
after Resection of all Gross Tumor, Phase II

KEYWORDS: germ cell tumors, chemotherapy, VAC

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effect of combined prophylactic vincristine, dactinomycin and cyclophosphamide (VAC) chemotherapy in patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (grade 2 and 3), choriocarcinoma, and malignant mixed germ cell tumors of the ovaries, Stage I or II (and early Stage II) after total removal of all gross tumor.

TECHNICAL APPROACH

Histologically confirmed malignant germ cell tumors of the ovary, Stages I or II, if previously untreated and completely resected, excluding patients with pure dysgerminoma (unless classified as anaplastic) are eligible for the protocol. Patients with grade 2 or 3 immature teratoma are eligible. Patients with early Stage III disease will be accepted if all gross tumor is resected.

PRIOR AND CURRENT PROGRESS

GOG 44 was originally closed in 1986, with 113 entries into this protocol. This protocol was reopened in April 1990 to continue follow-up of three patients only. Since that time, these three patients have been lost to follow-up; therefore, this protocol is completed.

CONCLUSIONS

VAC is an active regimen. In the majority of women, six to nine courses will prevent recurrence of malignant germ cell tumors of the ovary.

REPORT DATE: 08/31/91

WORK UNIT # 4287

DETAIL SUMMARY SHEET

TITLE: GOG 45 Evaluation of Vinblastine, Bleomycin and Cisplatin in Stage III and IV and Recurrent Malignant Germ Cell Tumors of the Ovary

KEYWORDS: germ cell tumors, VBP, chemotherapy

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology
SERVICE: Gynecologic Oncology Group

STATUS: Completed
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effect of four cycles of combined vinblastine, bleomycin and cisplatin (VBP) chemotherapy in the management of patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (all grades), choriocarcinoma, and malignant mixed germ tumors of the ovary with advanced or recurrent disease, incompletely resected. To evaluate the role of serum markers, especially alpha-fetoprotein and human chorionic gonadotropin, when they are present.

TECHNICAL APPROACH

Patients with histologically confirmed malignant germ cell tumors of the ovary of advanced Stage (III and IV) or recurrent disease, incompletely resected, are eligible. Patients with incompletely resected Stage II disease are eligible. Patients previously treated with VAC are eligible.

PRIOR AND CURRENT PROGRESS

This protocol was closed to patient accrual in September 1986. Total entries for the entire GOG was 111. This protocol was reopened in April 1990 to continue follow-up of three patients only. Since that time, these three patients have been lost to follow-up; therefore, this protocol is closed.

CONCLUSIONS

VBP will induce a substantial number of durable, complete responses even in patients having undergone prior chemotherapy. Toxicity is substantial. Disease extent is related to prognosis. For failing patients, subsequent therapy (VC or platinum + VP-16) will occasionally result in long disease-free survival.

REPORT DATE: 07/01/91

WORK UNIT # 4288

DETAIL SUMMARY SHEET

TITLE: GOG 49 A Surgical Pathologic Study of Women with Invasive Carcinoma of the Cervix Stage IB and Randomly Assigned Radiation Therapy

KEYWORDS: FIGO, carcinoma, cervix

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine, by observations of the 5-year survival and disease-free interval, the validity of current FIGO staging to the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in mm, histology and grade, growth pattern, and site and number of positive lymph nodes in Stage IB carcinoma of the cervix.

TECHNICAL APPROACH

All patients with primary, previously untreated, histologically confirmed invasive carcinoma of the cervix (squamous cell, adenocarcinoma, or adenosquamous) are eligible for this study.

PRIOR AND CURRENT PROGRESS

There are no conclusions regarding the randomized portion of this study due to poor accrual. Protocol was closed and terminated in October 1990.

CONCLUSIONS

The analysis of node status and the surgical pathologic factors has confirmed many traditional risk factors, as well as identified additional factors through multivariate analysis.

REPORT DATE: 11/04/91

WORK UNIT # 4289

DETAIL SUMMARY SHEET

TITLE: GOG 52 A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Vs. Cyclophosphamide Plus Platinol in Patients with Optimal Stage III Ovarian Adenocarcinoma

KEYWORDS: adenocarcinoma, ovarian

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine in optimal Stage II ovarian adenocarcinoma if addition of Adriamycin to cyclophosphamide plus cisplatin improves progression-free interval; frequency of negative, second look laparotomy; and survival.

TECHNICAL APPROACH

After debulking surgery for Stage III ovarian adenocarcinoma, patient is noted to have optimal disease if less than 1 cm in any one area is noted. They are then randomized to CAP versus CP every 3 weeks for eight courses. Depending upon response, patient will continue therapy off or on protocol.

PRIOR AND CURRENT PROGRESS

GOG 52 was closed in 1985, with a total of 415 patients entered into the protocol for the entire GOG. Seventeen patients were entered from WRAMC. This protocol was reopened in April 1990 to continue follow-up only on two patients. Since that time, these two patients have been lost to follow-up; therefore, this protocol is closed.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4290

DETAIL SUMMARY SHEET

TITLE: GOG 56 A Randomized Comparison of Hydroxyurea Vs. Misonidazole as an Adjunct to Radiation Therapy in Patients with Stage IIB, III, and IVA Carcinoma of the Cervix and Negative Paraaortic Nodes

KEYWORDS: radiation therapy, cervical carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether hydroxyurea or misonidazole is superior as a potentiator of radiation therapy in advanced cervical cancer.

TECHNICAL APPROACH

Patients with stages IIB, III and IVA cervical carcinoma confined to the pelvis will have noninvasive staging by CAT scan, sonography, or lymphangiogram. Histological evaluation of the nodes will either be done by percutaneous needle biopsy or surgical staging. Patients with negative nodes will be randomized to receive either misonidazole and pelvic irradiation or hydroxyurea and pelvic irradiation.

PRIOR AND CURRENT PROGRESS

This protocol was closed to patient accrual in December 1985 and terminated in July 1991.

CONCLUSIONS

Although it is inconclusive that hydroxyurea with radiotherapy is superior to misonidazole with radiotherapy, it appears that hydroxyurea is the more appropriate potentiator in patients with bulking cervix cancer. Hydroxyurea will remain the control potentiator for future randomized studies.

REPORT DATE: 07/01/91

WORK UNIT # 4292

DETAIL SUMMARY SHEET

TITLE: GOG 26HH A Phase II Trial of 5-Fluorouracil and Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies

KEYWORDS: 5-fluorouracil, pelvic, malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecologic Oncology Group

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of 5-fluorouracil (5-FU) and leucovorin in advanced metastatic or recurrent pelvic malignancies.

TECHNICAL APPROACH

Patients with histologically confirmed advanced, persistent, metastatic, or local gynecologic cancer with documented disease progression will be eligible. Leucovorin will be administered in a dose of 20 mg/m² daily x 5 days and repeated at 4 and 8 weeks and thereafter every 5 weeks. 5-FU will be administered in a dose of 425 mg/m² daily x 5 days to infuse immediately after the leucovorin has been given and will be repeated at 4 and 8 weeks and thereafter every 5 weeks.

PRIOR AND CURRENT PROGRESS

To date, 49 patients have been accrued by the entire GOG. Walter Reed has entered no patients. Three grade 4 neutropenias have been reported. No treatment-related deaths have been reported.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4293

DETAIL SUMMARY SHEET

TITLE: GOG 76S A Phase II Trial of Taxol in Patients with Advanced Cervical Carcinoma

KEYWORDS: Taxol, cervical carcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Completed
SERVICE: Gynecologic Oncology Group APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of Taxol on the treatment of patients with advanced cervical carcinoma.

TECHNICAL APPROACH

Patients with histologically confirmed, advanced, persistent, or recurrent squamous cell carcinoma of the cervix with documented disease progression after local therapy are eligible.

PRIOR AND CURRENT PROGRESS

Thirty-two patients were accrued by the entire GOG. No patients were entered from Walter Reed. This study was approved at WRAMC and closed by the Oncology Group simultaneously in May 1990.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4294

DETAIL SUMMARY SHEET

TITLE: GOG 8803 Flow Cytometrically Determined Tumor DNA Content in Advanced Epithelial Ovarian Cancer

KEYWORDS: flow cytometry, DNA, ovarian cancer

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Bosscher, James LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if tumor ploidy and cell proliferation can be correlated to various tumor and host factors, tumor responses, second look laparotomy findings, relapse and patient survival. To determine if tumor ploidy and cell proliferation are consistent between primary and metastatic sites and if they remain stable before and after chemotherapy.

TECHNICAL APPROACH

Patients with advanced (Stage III or IV) epithelial ovarian cancer that were previously entered on GOG Protocols 47, 52, or 60 will be eligible. In addition, patients must have received enough chemotherapy on protocol to be evaluable for response, have a paraffin-embedded ovarian tumor specimen from the pretreatment laparotomy available for use, and have adequate follow-up information available to include second-look laparotomy findings.

PRIOR AND CURRENT PROGRESS

Two hundred and fifty-four patients have been entered for the entire GOG. No patients from Walter Reed Army Medical Center have been entered.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4295

DETAIL SUMMARY SHEET

TITLE: GOG 8809 Flow Cytometrically Determined Tumor DNA Content in Ovarian Tumors of Low Malignant Potential

KEYWORDS: flow cytometry, DNA, ovarian tumors

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Bosscher, James LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether the DNA content of borderline ovarian tumors can be correlated with extent/stage of the tumor, potential for recurrence, and patient survival.

TECHNICAL APPROACH

Patients previously entered on GOG Protocol 72 with all stages of ovarian tumors of low malignant potential (any histologic type) can be entered. In addition, one paraffin-embedded specimen from pretreatment laparotomy and adequate follow-up information, to include second-look laparotomy findings or time to progression, must be available.

PRIOR AND CURRENT PROGRESS

Eighty-six patients have been entered for the entire GOG. Two patients have been entered from Walter Reed Army Medical Center.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4296

DETAIL SUMMARY SHEET

TITLE: GOG 8810 Flow Cytometrically Determined DNA Content in Endometrial Carcinoma

KEYWORDS: flow cytometry, DNA, adenocarcinoma

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Bosscher, James LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the DNA content of primary, recurrent and metastatic endometrial adenocarcinoma, and to identify whether the presence of aneuploid cell populations is related to histologic cell type, or grade or Stage of the tumor, lymph node or distant metastasis, progression free interval, or survival. To determine whether tumor ploidy is consistent between primary tumors and their metastasis.

TECHNICAL APPROACH

Patients are eligible if previously entered on GOG Protocol 33, and if a paraffin block sample from the D&C or hysterectomy is available. If metastatic tumor is present, one paraffin block of the metastatic tumor would be highly desirable.

PRIOR AND CURRENT PROGRESS

Two hundred and thirty-four patients have been entered for the entire GOG. Five patients have been entered by Walter Reed Army Medical Center.

CONCLUSIONS

Too early.

REPORT DATE: 07/25/91

WORK UNIT # 4298

DETAIL SUMMARY SHEET

TITLE: GOG 111 A Phase III Randomized Study of Cyclophosphamide and Cisplatin
Vs. Taxol and Cisplatin in Patients with Suboptimal Stage III and Stage
IV Epithelial Ovarian Carcinoma

KEYWORDS: ovarian carcinoma, cisplatin, Taxol

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC
ASSOCIATES: Bosscher, James LTC MC

DEPARTMENT: Department of Obstetrics and Gynecology STATUS: Ongoing
SERVICE: Gynecologic Oncology Group APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine rate, response duration and survival in suboptimal Stage III and Stage IV ovarian cancer treated with two different platinum-based combination chemotherapy regimens. To compare the relative toxicities of the two regimens.

TECHNICAL APPROACH

Patients with established ovarian epithelial cancer, suboptimal (1 cm in diameter) Stage III or Stage IV, are eligible. All patients must have optimal surgery for ovarian cancer. The following histologically confirmed ovarian malignancies are eligible: serous adenocarcinoma, mucinous adenocarcinoma, clear-cell adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, and mixed epithelial carcinoma.

PRIOR AND CURRENT PROGRESS

There have been a total of 183 patients entered into this protocol for the entire GOG. Seven patients have been entered from Walter Reed (four pending, three evaluable). There have been 73 grade 4 leukopenias, one grade 4 anemia, and one grade 4 cardiac toxicity noted. This protocol remains open.

CONCLUSIONS

Too early.

REPORT DATE: 07/01/91

WORK UNIT # 4291

DETAIL SUMMARY SHEET

TITLE: GOG 26GG A Phase II Trial of Fazarabine in Patients with Advanced or Recurrent Pelvic Malignancies

KEYWORDS: Fazarabine, pelvic, malignancies

PRINCIPAL INVESTIGATOR: Barnhill, Danny LTC MC

ASSOCIATES: Park, Robert MD

DEPARTMENT: Department of Obstetrics and Gynecology

STATUS: Ongoing

SERVICE: Gynecological Oncology Group

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of Fazarabine in the treatment of advanced or recurrent gynecologic cancers refractory to curative therapy or established treatments.

TECHNICAL APPROACH

Patients with histologically confirmed gynecologic cancer either recurrent or advanced on initial presentation and refractory to curative therapy or established treatments will be eligible. The patients will be treated with Fazarabine at the dosage of 30 mg/m²/day for 5 days. Cycles of therapy will be repeated every 28 days.

PRIOR AND CURRENT PROGRESS

To date, 45 patients have been accrued by the entire GOG. Walter Reed has entered one patient. Two cases of grade 4 neutropenia have been reported. No treatment related deaths have been reported.

CONCLUSIONS

Too early.

REPORT DATE: 03/27/91

WORK UNIT # 4805

DETAIL SUMMARY SHEET

TITLE: The Effects of Selected Medications on In Vitro and In Vivo Red Cell Survival

KEYWORDS: transfusion reaction, flow cytometry

PRINCIPAL INVESTIGATOR: Smith, Henry CPT BS

ASSOCIATES: Hathaway, Thomas LTC MS

DEPARTMENT: Department of Pathology and Area Laboratories STATUS: Completed

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To demonstrate the relative compatibility of different medications when transfused simultaneously with blood, and to determine the red cell survival in dogs using fluorescence lipophilic probe, when an autologous sample is infused simultaneously with selected medications.

TECHNICAL APPROACH

In vitro studies - mix medications with blood and determine destruction. In vivo study - transfuse six dogs with medication/blood mixture to determine cell survival.

PRIOR AND CURRENT PROGRESS

Work on this protocol has been completed. It was approved by the Animal Use Committee and the Clinical Investigation Committee, December 1989, and successfully defended at the Graduate School of Bowling Green University, Bowling Green, Ohio for the completion of the principal investigator's fellowship at Walter Reed Army Medical Center.

CONCLUSIONS

Certain medication demonstrated in vitro cell destruction when tested in the in vivo model. None of the dogs tested show significant reduction of cell survival after transfusion.

DETAIL SUMMARY SHEET

TITLE: Reticulocyte Maturation in Anticoagulated Blood Determined by Flow Cytometry

KEYWORDS: reticulocyte, flow cytometry, stored blood

PRINCIPAL INVESTIGATOR: Perry, Elaine CPT MS

ASSOCIATES: Lippert, Lloyd LTC MS; Salata, Kalman PhD

DEPARTMENT: Department of Pathology and Area Laboratories STATUS: Completed

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 6,821 Previous FYs: \$ 0 Total: \$ 6,821

STUDY OBJECTIVE

To determine reticulocyte (RE) persistence in stored donor blood and donor RE persistence in post transfusion specimens.

TECHNICAL APPROACH

Three methods were employed to quantify RE: 1) manual new methylene blue and flow cytometric analysis (FCA) methods, 2) the Becton Dickinson FACStar with thiazole orange (TO) and 3) the Sysmex R-1000 with auromine O (AO). Aliquots were stored at 4, 24 and 37 degrees C and RE persistence was analyzed at timed intervals. TO staining cells, sorted by flow cytometry, were analyzed by transmission electron microscopy (TEM) to confirm presence of mitochondria and ribosomes. Two color FCA RE phenotyping was used to follow donor reticulocytes immediately after transfusion (0 hour), 3, 6, 12, 24, 48 and 72 hours post transfusion.

PRIOR AND CURRENT PROGRESS

FCA using TO demonstrated RE numbers remained unchanged for 35 days in units of CPDA-1 blood at 4 degrees C. TEM of TO staining cells sorted by flow cytometry confirmed presence of mitochondria and ribosomes, RE hallmarks. RE levels in blood stored at 24 and 72 degrees C had disappeared by Day 13 and Day 6 respectively. Detailed in vitro RE studies at 37 degrees C found approximately 50% of the RE disappeared in 4 hours and by 72 hours they were essentially undetectable. In transfused patients, 50% had observable donor RE through 48 hours and in some cases through 72 hours. Different donor RE survival rates were observed in this study, which primarily dealt with patients with abnormal hematologic status, and that of a previous investigator (Griffin), which looked at surgical patients. It appears patient condition and treatment may have an impact on donor RE survival.

CONCLUSIONS

1) RE is stable over the life of a CPDA-1 unit of blood (35 days) at 4 degrees C. 2) RE stability in anticoagulated blood is temperature dependent. 3) In transfused patients, donor RE can persist through 72 hours post transfusion and caution needs to be taken when interpreting RE values or performing mixed cell population separation techniques based on RE density from samples drawn within 72 hours of transfusion.

DETAIL SUMMARY SHEET

TITLE: Reference Ranges of Alpha Fetoprotein and Human Chorionic Gonadotrophin
in Cerebrospinal Fluid

KEYWORDS: alpha fetoprotein, cerebrospinal fluid, HCG

PRINCIPAL INVESTIGATOR: Kuenstner, Todd MAJ MC

ASSOCIATES: Ciment, Peter LTC MS

DEPARTMENT: Department of Pathology and Area Laboratories STATUS: Completed

APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine reference ranges of alpha fetoprotein and human chorionic gonadotrophin (HCG) in cerebrospinal fluid.

TECHNICAL APPROACH

Specimens will be obtained from patients who are undergoing spinal anesthesia. The tests will be done with an ELISA methodology on the Abbott Quantum Analyzer.

PRIOR AND CURRENT PROGRESS

The first year's progress on this protocol consisted of obtaining administrative approval from the research committees of Walter Reed Army Medical Center, National Naval Medical Center in Bethesda, and Veterans Administration Hospital of Washington, DC. Additionally, a Memo of Understanding was initiated for completion by each institution. The PI left the Army, however, in September 1991, and the Associate Investigator is unable to continue the study. No specimens were collected.

CONCLUSIONS

None.

REPORT DATE: 07/30/91

WORK UNIT # 6038

DETAIL SUMMARY SHEET

TITLE: Collection and Cryopreservation of Spleen Cells for the Production of Monoclonal Antibodies

KEYWORDS: spleen, cryopreservation, lymphocyte

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Apr 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To use cryopreserved spleen cells from a bank as a source of growth factors and tumor monoclonal antibodies.

TECHNICAL APPROACH

After splenectomy, spleen is dissected and single cell suspensions are made. These cells are cryopreserved in liquid nitrogen for later use.

PRIOR AND CURRENT PROGRESS

Pediatric Hematology-Oncology Service has not used stored cells in any projects during the reporting year. The Pediatric Infectious Disease Service has expressed interest in using the cells, and the Chief of the Service has been approached about becoming the principal investigator for this study. Reply pending.

CONCLUSIONS

Study should remain open.

REPORT DATE: 09/12/91

WORK UNIT # 6051

DETAIL SUMMARY SHEET

TITLE: Effect of Adrenarchal Stage on Treatment of Precocious Puberty with
Leuprolide, a GnRH Analogue

KEYWORDS: precocious puberty, GnRH, adrenarche

PRINCIPAL INVESTIGATOR: Poth, Merrily MD
ASSOCIATES: Francis, Gary MD; Newman, Robert MD

DEPARTMENT: Department of Pediatrics

STATUS: Completed
APPROVAL DATE: Nov 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

The objective of this study is to determine whether the adrenarcheal stage of the patient at the time of institution of treatment for precocious puberty is important to the outcome of therapy.

TECHNICAL APPROACH

Patients with central precocious puberty who are designated for GnRH therapy have adrenarcheal staging done using physical examination (Tanner Staging) and serum DHEAS level. During therapy, the effects of treatment (i.e. the cessation of pubertal progression, suppression of gonadotropin, and bone age and growth rate with consequent change in projected adult height) are determined. Analysis will be made to determine whether lateness of adrenarcheal stage compromises the effectiveness of therapy with GnRH analogues.

PRIOR AND CURRENT PROGRESS

Only 3 of the 21 patients enrolled in this protocol remain on therapy. We will not place additional patients on the protocol but will continue to follow all patients through puberty if possible.

CONCLUSIONS

GnRH analogue therapy is an effective way of halting progression of central precocious puberty. No complications of therapy have been noted to date.

REPORT DATE: 11/12/91

WORK UNIT # 6059

DETAIL SUMMARY SHEET

TITLE: Malondialdehyde Production by Neonatal Erythrocytes

KEYWORDS: vitamin E, free radicals, neonate

PRINCIPAL INVESTIGATOR: Poth, Merrily MD

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

APPROVAL DATE: Sep 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 3,031 Total: \$ 3,031

STUDY OBJECTIVE

The objective of this study is to determine whether free radical production of red blood cell membranes of neonates would reflect vitamin E deficiency in this population.

TECHNICAL APPROACH

Neonatal red blood cells were exposed to hydrogen peroxide and malondialdehyde (MDA) production measured to attempt to determine whether this measure of vitamin E sufficiency/deficiency would help to resolve the questioned need for vitamin E supplement of newborns, individually or as a group.

PRIOR AND CURRENT PROGRESS

No work has taken place this calendar year. Prior work by our group showed that many newborn infants showed increased MDA production by RBC's and that this persisted for variable periods of time. We hope to continue the project this year and begin to explore the association of increased MDA production with neonatal morbidity.

CONCLUSIONS

Many newborn infants show increased MDA production by RBC's as a measure of functional vitamin E deficiency. It remains to be tested whether this "deficiency" places these infants at increased risk for neonatal complications, such as necrotizing enterocolitis, retinopathy, or prematurity.

REPORT DATE: 06/28/91

WORK UNIT # 6061

DETAIL SUMMARY SHEET

TITLE: Granulopoiesis and Megakaryocytopoiesis in Human Cord Blood

KEYWORDS: megakaryocytopoiesis, interleukin-1, granulopoiesis

PRINCIPAL INVESTIGATOR: Edwards, Erwood MAJ MC

ASSOCIATES: Olson, Thomas MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 456 Previous FYs: \$ 317 Total: \$ 773

STUDY OBJECTIVE

To characterize granulocyte and megakaryocyte progenitors in the preterm and term infant.

TECHNICAL APPROACH

Cord blood is collected and the mononuclear cells are used for progenitor assays or measurement of interleukin 1.

PRIOR AND CURRENT PROGRESS

Results from 10-15 cord blood samples have shown increased numbers of megakaryocyte progenitors compared to adult blood and bone marrow. The progenitors in cord blood also appear less responsive to megakaryocyte colony stimulating factor than adult megakaryocyte progenitors.

CONCLUSIONS

None.

REPORT DATE: 04/20/91

WORK UNIT # 6063

DETAIL SUMMARY SHEET

TITLE: The Effect of Mestinson on Growth in Non-growth Hormone Deficient Short Children

KEYWORDS: short stature, growth hormone, pyridostigmine

PRINCIPAL INVESTIGATOR: Newman, Robert MAJ MC

ASSOCIATES: Poth, Merrily MD

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Feb 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether mestinson (pyridostigmine) has physiological effect on growth hormone secretion and hence on growth.

TECHNICAL APPROACH

Mestinson, 60 mg (or placebo), given at bedtime each night to short, non-growth hormone deficient children. Growth rate and serum somatomedin C levels will be compared for placebo versus drug treatment time periods.

PRIOR AND CURRENT PROGRESS

A total of seven patients have been enrolled in the study, six of whom have completed both the experimental and placebo phases. Although the numbers are small, it appears that there are no differences in growth velocity, serum IGF-1, or bone age advancement between pyridostigmine and placebo treatment phases. Several more patients will be required before definitive conclusions can be made. Two patients have been enrolled within the prior year. There have been no serious or unexpected adverse reactions. No patients have been withdrawn from the study.

CONCLUSIONS

More patients are required before conclusions can be made regarding the efficacy of pyridostigmine upon the stimulation of growth.

REPORT DATE: 07/25/91

WORK UNIT # 6064

DETAIL SUMMARY SHEET

TITLE: The Effect of Somatomedin C on Androgen Receptor and 5-a-reductase Activities in a Hormonally Responsive Tissue, the Penile Foreskin

KEYWORDS: somatomedin C, androgen, 5-alpha-reductase

PRINCIPAL INVESTIGATOR: Francis, Gary LTC MC
ASSOCIATES: Poth, Merrily MD; Dykstra, Kenneth

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 4,100 Previous FYs: \$ 5,054 Total: \$ 9,154

STUDY OBJECTIVE

This study is designed to determine whether or not growth hormone acting through its effector hormone, somatomedin C (IGF1), has in vitro effects on androgen receptor activity or 5-alpha-reductase activity in the penile foreskin.

TECHNICAL APPROACH

Primary explant fibroblast cultures will be prepared from five normal infant foreskins at the time of routine circumcision. Confluent monolayer cultures will be used to assay 5-alpha-reductase activity by the conversion 3H-testosterone to H-dihydrotestosterone and metabolites, as well as androgen receptor activity assayed by specific binding of 3H-dihydrotestosterone to whole cell preparations.

PRIOR AND CURRENT PROGRESS

IGF1, in vitro, appears to increase the protein and DNA content of fibroblast cultures. This effect, however, appears to only be present when androgen is also added to the cultures. Androgen alone has no effect. IGF1 does not appear to directly change the activity of 5-alpha-reductase or androgen receptors. Currently, our laboratory is investigating whether or not these preliminary observations are true under different experimental conditions and whether or not thymidine incorporation into DNA is also increased. In addition, we are evaluating whether or not GH augments the effects of IGF1 or can replace it altogether.

CONCLUSIONS

IGF1 appears to affect neonatal foreskin fibroblasts by inducing a proliferative response but only in the presence of androgen. This does not appear in preliminary studies to be mediated through a change in either 5-alpha-reductase or androgen receptor activities.

REPORT DATE: 08/15/91

WORK UNIT # 6215

DETAIL SUMMARY SHEET

TITLE: The Enteral Absorption of Human IgG by the Neonatal Guinea Pig and Its Retention of Opsonic Activity Type III Group B Streptococcus

KEYWORDS: immunoglobulin, enteral absorption, guinea pig

PRINCIPAL INVESTIGATOR: Jesse, Steven CPT MC

ASSOCIATES: Weisman, Leonard LTC MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 8,545 Total: \$ 8,545

STUDY OBJECTIVE

The human newborn has been classically described as a "nonabsorber" of breastmilk antibody. Using an animal model which resembles the human neonate, (in a GI sense), we are attempting to demonstrate the absorption of Human IgG via the gut after gavaging the subject with a known amount of IgG shortly after birth. We also hope to identify variables which may influence enteral absorption of IgG.

TECHNICAL APPROACH

Vaginally delivered Hartley Guinea Pig pups are gavaged with a 10% human IgG preparation shortly after birth. Cohorts receive either 5 gm/kg or 1 gm/kg po either once or 3x. Controls receive either 5 gm/kg or 1 gm/kg ip xl. Serial blood samples (0.3cc) are then obtained via a femoral cutdown at 24, 48, and 72 hrs; and at 1 and 2 weeks after IgG administration. Pups remain with their dam and suckle ad lib; all being euthanized after 2 weeks. A Competitive Inhibition Enzyme Immunoassay is being used to compare serum human IgG levels in all animals, over time, and between 5g/kg and 1g/kg groups.

PRIOR AND CURRENT PROGRESS

Animal and laboratory work are completed. Analysis is underway. Expect paper submission and publication this coming fiscal year.

CONCLUSIONS

None yet.

REPORT DATE: 08/27/91

WORK UNIT # 6219

DETAIL SUMMARY SHEET

TITLE: Chronic Stress, Change in Social Support, and Uncertainty

KEYWORDS: chronic stress, reactions to stress

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To evaluate psychological, physiological, and behavioral responses to ongoing chronic stress; b) To examine the role of change in the stress-social support relationship; and c) To determine the role of ambiguity or uncertainty in stress.

TECHNICAL APPROACH

A multi-modal (endocrine, hematologic, psychiatric, immunologic) evaluation is used for family members of children with malignancies. This study is in conjunction with the Department of Psychiatry USUHS. Families are screened by a hematology-oncology nurse specialist.

PRIOR AND CURRENT PROGRESS

Accrual continues. MAJ McFarland reports that 38 families with a child who has cancer have been asked to volunteer in this study (8 families refused) since its approval date. Dr. Baum has been contacted about any progress he has made in this reporting period; reply pending. He also has been asked to provide accrual statistics each July that this study is open.

CONCLUSIONS

Study should remain open.

REPORT DATE: 04/01/91

WORK UNIT # 6223

DETAIL SUMMARY SHEET

TITLE: Ceftriaxone for Outpatient Management of Suspected Occult Bacteremia: A Multicenter Cooperative Study

KEYWORDS: occult, bacteremia, ceftriaxone

PRINCIPAL INVESTIGATOR: Robb, Merlin MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare ceftriaxone and augmentin in the treatment of febrile infants and children who have no obvious focus of infection and who, therefore, may have occult bacteremia. This is a collaborative, multicenter study with Colonel James Bass serving as study monitor.

TECHNICAL APPROACH

Patients fulfilling study entry criteria and consenting to study are evaluated for occult bacteremia with blood cultures, exam and other studies as indicated. They are then randomized to therapy with either augmentin PO or ceftriaxone IM and a follow-up exam is performed 24 hours later. Further evaluation and therapy varies according to symptoms and blood culture results. Data sheets are compiled at entry and for each follow-up. Patients with positive blood cultures will form the study group for comparing the two antibiotic regimens.

PRIOR AND CURRENT PROGRESS

A total of eight patients have been enrolled in the study protocol to date. The failure to acquire new patients into the study is multifactorial but rests primarily with the failure of the current PI to adequately advertise the protocol among primary pediatric health care providers. This failure is due in part to reassignment of the PI to a location off the WRAMC campus. It is not anticipated that WRAMC will provide many patients to this study due to the relatively small size of our primary care patient population. In order to optimize our contribution, COL Peter Zawadsky will become the PI for this project, effective 01 Apr 91.

CONCLUSIONS

The collaborative project continues to enroll patients but has not yet achieved sufficient numbers of bacteremic patients to analyze the data.

REPORT DATE: 08/14/91

WORK UNIT # 6231

DETAIL SUMMARY SHEET

TITLE: Advanced Airway Management Skill Station Using Cats

KEYWORDS: endotracheal, intubation, cats

PRINCIPAL INVESTIGATOR: Restuccia, Robert LTC MC

ASSOCIATES: Bley, John Jr. MAJ VC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To teach orotracheal intubation to pediatricians and pediatric nurses attending the Pediatric Advanced Life Support Course at Walter Reed Army Medical Center. Using live cats enables the students to practice on a model which simulates intubation of infants and children.

TECHNICAL APPROACH

Cats are anesthetized with ketamine in order to permit orotracheal intubation while maintaining spontaneous respiration. If needed, the cats receive topical lidocaine on their vocal cords to diminish laryngospasm and intramuscular atropine to reduce airway secretions. Each cat is limited to five attempted orotracheal intubations, after which it is returned to the holding cage and monitored until it recovers from anesthesia.

PRIOR AND CURRENT PROGRESS

Since the approval of this training protocol in February 1989, we have conducted six Pediatric Advanced Life Support Courses at WRAMC. Each course has included the "cat intubation laboratory," and 16 cats have been anesthetized for each laboratory. All the cats have tolerated the intubation without a single complication and recovered from anesthesia.

CONCLUSIONS

The "cat intubation laboratory" has been very successful in achieving its goal of training pediatric health care providers in the proper technique of intubation for infants. The humane treatment of the animals is confirmed by the complete recovery of all of them from anesthesia and intubation. We expect to continue to conduct this training laboratory three times each year.

REPORT DATE: 09/26/91

WORK UNIT # 6239

DETAIL SUMMARY SHEET

TITLE: Microbiology of Otitis Media in Immunocompromised Pediatric Patients

KEYWORDS: immunocompromised, otitis media, microbiology

PRINCIPAL INVESTIGATOR: Zawadsky, Peter COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define the microbiology of otitis media in immunocompromised patients.

TECHNICAL APPROACH

Immunocompromised patients with documented otitis media with effusion undergo a diagnostic tympanocentesis. The resulting specimen is evaluated microbiologically by the laboratory, and therapy is tailored to the culture results.

PRIOR AND CURRENT PROGRESS

This study is being terminated due to lack of registrants. This has occurred mostly because physicians prefer not to use an invasive protocol for a disease whose outcome is usually good. This disease occurs acutely and usually not during the hospital's "working day," so it has not been possible to overcome physician bias by explaining the relevance of volunteering along with presenting the implications of participating. Also, the potential registrant population is small.

CONCLUSIONS

Study should be closed.

REPORT DATE: 06/17/91

WORK UNIT # 6240

DETAIL SUMMARY SHEET

TITLE: A Prospective Study of Short Vs. Long Course Antibiotic Therapy for Central Venous Catheter Infections in Pediatric Patients

KEYWORDS: infection, antibiotic therapy, central venous catheter

PRINCIPAL INVESTIGATOR: Robb, Merlin MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare two durations of therapy for central venous catheter (CVC) infections, with short-term outcome and relapse as study endpoints.

TECHNICAL APPROACH

Patients are eligible for the study if they have documented systemic (i.e., blood) or local (i.e., exit wound) infection and have a long-term, in-dwelling central venous catheter. The systemic and local groups are randomized independently to long or short therapy. Endpoints include failure to clear infection at specified duration of therapy and relapse.

PRIOR AND CURRENT PROGRESS

A total of three patients have been enrolled in the exit wound portion of the protocol, and an additional eight patients were enrolled in the systemic infection portion of the protocol. Of the eight patients enrolled and completing the systemic therapy protocol, one was removed from analysis due to an alteration in antibiotic useage which was inconsistent with protocol requirements. The slow enrollment in this protocol is being addressed by the appointment of a new principal investigator who can identify protocol candidates on a daily basis.

CONCLUSIONS

Thus far, protocol has not acquired sufficient participants to make analysis meaningful. However, sufficient patients are available to achieve the goals of this study, and the protocol will be reviewed with the pediatric hematology-oncology group to assure maximum enrollment.

REPORT DATE: 06/03/91

WORK UNIT # 6241

DETAIL SUMMARY SHEET

TITLE: Staphylococcal Aureus Colonization Following Neonatal Circumcision: Is There Device Dependency?

KEYWORDS: staphylococcal aureus, circumcision

PRINCIPAL INVESTIGATOR: Wiswell, Thomas LTC MC

ASSOCIATES: Curtis, Jerri LCDR MC; Dobek, Arthur PhD

DEPARTMENT: Department of Pediatrics

STATUS: Completed

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 143 Previous FYs: \$ 2,920 Total: \$ 3,063

STUDY OBJECTIVE

To determine if male infants are more likely to be colonized with staphylococcal aureus following circumcision with a plastic clamp compared with a metal clamp.

TECHNICAL APPROACH

We are randomizing circumcision with either the Plastibell (plastic) or the Gomco (metal) clamps. Cultures are then obtained 24 hours later, as well as at the 2 week well baby check. These specimens are evaluated to determine the specific type of staphylococci which are growing, as well as coagulase positivity/negativity. For the bacteriologic identification we are using STAPH IDENT and STAPH TRAC kits; while for coagulase testing we are using REMEL's agglutination technique. In addition, we are examining for staphylococcal page types. Charles Zierdt, Ph.D., from NIH assisted us with identification.

PRIOR AND CURRENT PROGRESS

Patient enrollment (total 123) was completed in June 1990. There were no adverse reactions to patients. There was no benefit to patients with the staphylococcal colonization virtually identical in both groups. A manuscript will be published in the June 1991 issue of The Journal of Pediatrics. This work was the runner-up for the Andrew Margileth Award at the Annual Uniformed Services Pediatric Seminar, Monterey, California. It will be presented at the annual meeting of the American Academy of Pediatrics in October 1991 (New Orleans).

CONCLUSIONS

Staphylococcal aureus colonization following circumcision is not device-dependent.

REPORT DATE: 08/15/91

WORK UNIT # 6245

DETAIL SUMMARY SHEET

TITLE: The Effect of Asphyxia on the Susceptibility of the Suckling Rat Pup to Group B Streptococcal Infection

KEYWORDS: group B streptococcal, asphyxia, neonate

PRINCIPAL INVESTIGATOR: Beachy, Joanna MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,878 Total: \$ 1,878

STUDY OBJECTIVE

To determine if asphyxia affects bacteremia and mortality of group B streptococcal (GBS) infected suckling rats and if the mechanism is mediated via neutrophil number or function. To determine if asphyxia affects bacteremia in the adult rat, and if so, whether the mechanism is mediated via neutrophil number or function.

TECHNICAL APPROACH

Previously established laboratory techniques will be used to evaluate the question in the suckling rat. Specifically, a suckling rat model of GBS sepsis will be used to evaluate bacteremia and mortality following infection with and without asphyxia. Asphyxial methods have been worked out on previous protocols. Previously reported methods of neutrophil number and function will be used to evaluate the affect of asphyxia in vitro. Adult animal model will be developed to evaluate the similar question addressed in neonatal rats.

PRIOR AND CURRENT PROGRESS

All laboratory work has been completed and analysis is underway. Expect submission of papers in coming fiscal year.

CONCLUSIONS

None yet.

REPORT DATE: 08/23/91

WORK UNIT # 6246

DETAIL SUMMARY SHEET

TITLE: The Use of Multiple Site Blood Cultures in the Evaluation and Management of Sepsis Neonatorum

KEYWORDS: blood culture, neonate, septicemia

PRINCIPAL INVESTIGATOR: Wiswell, Thomas LTC MC

ASSOCIATES: Hachey, Wayne CPT MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 232 Previous FYs: \$ 0 Total: \$ 232

STUDY OBJECTIVE

To see if multiple site blood cultures, rather than a single site set of cultures, would provide enough additional information to recommend their general use in the nursery for evaluation of suspected bacteremia.

TECHNICAL APPROACH

The approach at WRAMC has apparently been to use multiple rather than single site cultures (in contrast to published literature). Thus, we reviewed the inpatient medical records of all inborn neonates who were evaluated for suspected sepsis during the first week of life during the period 1987-1989. We used a "scoring" sheet to collect information from each chart.

PRIOR AND CURRENT PROGRESS

Study is complete, resulting in two publications.

CONCLUSIONS

Multiple site blood cultures provide additional important information regarding infants with "true" sepsis and those with contaminated cultures. The use of various hematologic parameters, as well as the urine latex particle agglutination test for group B streptococcus, do not provide conclusive evidence of neonatal sepsis.

REPORT DATE: 04/08/91

WORK UNIT # 6254

DETAIL SUMMARY SHEET

TITLE: A Comparison of Electronic, Chemical and Infrared Thermometry and Anatomical Site Selection in a Pediatric Population

KEYWORDS: thermometry, Gold Standard, FirstTemp

PRINCIPAL INVESTIGATOR: White, Christopher MAJ MC

ASSOCIATES: Fletcher, Dale MAJ ANC; Robb, Merlin MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare temperature measurements obtained in a pediatric population using different instruments and different anatomical sites.

TECHNICAL APPROACH

Children presenting to the pediatric clinic at WRAMC will be asked to participate. The following temperature measurements will be taken: 1) Children less than 5 years - infrared thermometry, chemical-axillary, electronic-axillary, and electronic-rectal (the Gold Standard); 2) Children greater than 5 years - infrared thermometry, chemical-oral, and electronic-oral (Gold Standard). The following data will be compared and analyzed: 1) How well do the various methods identify fever compared to the Gold Standard?; 2) Do the test methods vary significantly from the Gold Standard, and how do they correlate with the Gold Standard? Infrared-thermometry - FirstTemp-tympanic, Chemical - TempaDOT, Electronic - IVAC.

PRIOR AND CURRENT PROGRESS

One hundred and twenty six children were entered into the study: 42% under 5 years old, and 58% greater than 5 years old. No serious or unexpected adverse reactions occurred during the study. Statistical analysis of the data has been completed, and no new patients have been enrolled since April 1990. The study has been completed.

CONCLUSIONS

Under 5 years old: The FirstTemp was highly sensitive and specific compared to rectal IVAC, while axillary IVAC and TempaDOT temperatures had lower sensitivities and specificities. Over 5 years old: The FirstTemp had a high specificity but low sensitivity and varied significantly compared to the Oral IVAC. The TempaDOT oral measurement showed a better correlation, sensitivity, and specificity compared to Oral IVAC temperatures.

REPORT DATE: 04/09/91

WORK UNIT # 6255

DETAIL SUMMARY SHEET

TITLE: Comparison of Diagnostic Methods for Respiratory Syncytial Virus in a Clinical Setting

KEYWORDS:

PRINCIPAL INVESTIGATOR: Bash, Margaret LCDR MC

DEPARTMENT: Department of Pediatrics

STATUS: Terminated
APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol has been administratively terminated.

TECHNICAL APPROACH

This protocol has been administratively terminated.

PRIOR AND CURRENT PROGRESS

This protocol has been administratively terminated.

CONCLUSIONS

This protocol has been administratively terminated.

REPORT DATE: 04/01/91

WORK UNIT # 6256

DETAIL SUMMARY SHEET

TITLE: The In Vitro Effect of Tumor Necrosis Factor on the Function of the Pituitary Gonadotrophs of the Rat

KEYWORDS: TNF, pituitary

PRINCIPAL INVESTIGATOR: Francis, Gary LTC MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 67 Previous FYs: \$ 0 Total: \$ 67

STUDY OBJECTIVE

To determine if tumor necrosis factor affects the secretion of LH from cultured pituitary cells of the rat.

TECHNICAL APPROACH

Pituitary cell cultures will be established from acutely dispersed cells. Fresh cells must be prepared for each experiment. Cells will be stimulated with GnRH and the LH released measured by Rat LH-RIA. TNF will be added in parallel experiments to determine if it blocks GnRH stimulated LH release.

PRIOR AND CURRENT PROGRESS

Materials for rat LH-RIA have been obtained from NIH. Iodination of rat LH for use in RIA is the next step, and we are ready to proceed once joint agreement with Dr. Paul Shaudies can be negotiated to allow use of iodinating facility.

CONCLUSIONS

Project is viable and ready to proceed.

REPORT DATE: 04/01/91

WORK UNIT # 6257

DETAIL SUMMARY SHEET

TITLE: The In Vitro Effect of Tumor Necrosis Factor on the Function of the Gonadal Axis of the Rat

KEYWORDS: TNF, gonad

PRINCIPAL INVESTIGATOR: Francis, Gary LTC MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 8,681 Previous FYs: \$ 0 Total: \$ 8,681

STUDY OBJECTIVE

To determine if tumor necrosis factor (TNF) has an effect on testosterone (T) production in the testis.

TECHNICAL APPROACH

Leydig cells will be separated and cultured from acutely dispersed testicular cell preparation. Cells will be incubated with hCG and TNF to determine if TNF inhibits T production.

PRIOR AND CURRENT PROGRESS

Two presented abstracts have identified that TNF (at multiple concentrations, with 0-48 preincubation) has no direct effect on T production nor does it block hCG stimulated T. However, TNF appears to induce formation of a factor in macrophages that subsequently blocks T production.

CONCLUSIONS

TNF appears to have no direct effect on T production but may induce a macrophage secretory product which does inhibit T. Current work is underway to evaluate what this factor might be.

REPORT DATE: 04/01/91

WORK UNIT # 6258

DETAIL SUMMARY SHEET

TITLE: Polymorphism of Prolactin in Neonatal Cord Blood

KEYWORDS: prolactic, neonatal

PRINCIPAL INVESTIGATOR: Francis, Gary LTC MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if prolactin (PRL) exists in multiple species in human cord blood, and, if so, whether or not these different species have different biological activity.

TECHNICAL APPROACH

Cord blood is to be collected from the placenta after delivery of the infant and after detachment from the mother. Serum will be separated and frozen for analysis over G-100 sephadex column chromatography. PRL will be identified by radioimmunoassay (RIA), and biological activity will be assessed by NB2 rat node lymphoma cell bioassay.

PRIOR AND CURRENT PROGRESS

To date, materials for performing column separation and RIA have been obtained. ObGyn, however, has not allowed any cord blood samples to be collected.

CONCLUSIONS

Project is still viable pending further discussions to allow access to cord blood.

REPORT DATE: 09/25/90

WORK UNIT # 6259

DETAIL SUMMARY SHEET

TITLE: EXOSURF Pediatric Sterile Powder Treatment IND Protocol EXO-501

KEYWORDS: surfactant, respiratory distress, newborn

PRINCIPAL INVESTIGATOR: Mendiola, Joe MAJ MC

ASSOCIATES: Wiswell, Thomas LTC MC; Beachy, Joanna MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the effect of a synthetic surfactant in newborn infants with or at high risk of surfactant deficiency.

TECHNICAL APPROACH

Newborn infants who meet established weight criteria and respiratory parameters are given either a single prophylactic dose of EXOSURF Pediatric or two doses of EXOSURF Pediatric to treat established Respiratory Distress Syndrome.

PRIOR AND CURRENT PROGRESS

EXOSURF Pediatric has been released for marketing by the FDA for prophylactic and rescue treatment of neonatal Respiratory Distress Syndrome. As a result, the Burroughs Wellcome Company initiated close-out procedures of the Treatment IND. All of the unused drug supplied under the Treatment IND has been returned. A total of eight patients were treated under the Treatment IND protocol.

CONCLUSIONS

Upon completion of analysis of the data on the approximately 10,000 patients enrolled nationwide, we will receive a report summarizing both the overall Treatment IND experience and our site specific experience.

REPORT DATE: 05/14/91

WORK UNIT # 6262

DETAIL SUMMARY SHEET

TITLE: Retrospective Comparison of Paired Isolator and BACTEC Blood Culture Systems

KEYWORDS: isolator, BACTEC, blood culture

PRINCIPAL INVESTIGATOR: Ascher, David MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed
APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if there is an increased yield of pathogenic isolates recovered by the isolator culture system compared to the BACTEC culture system, and to determine if there were significant differences between the culture systems in the specific pathogens recovered.

TECHNICAL APPROACH

Results from isolators and BACTEC blood culture submitted from children with central venous catheters and suspected sepsis will be reviewed.

PRIOR AND CURRENT PROGRESS

Nine hundred and thirteen (913) paired isolators and BACTEC blood cultures were identified in 91 pediatric patients with central venous catheters, with subsequent chart review.

CONCLUSIONS

The isolator and BACTEC systems in combined use were comparable in the isolation of individual pathogenic species. In combination, they were significantly better than either method alone.

REPORT DATE: 07/10/91

WORK UNIT # 6266

DETAIL SUMMARY SHEET

TITLE: High Dose Chemotherapy with Autologous Bone Marrow Rescue in Children with Recurrent or Progressive Solid Tumors or Primary CNS Malignancies, Phase II

KEYWORDS: autologous, marrow transplantation, solid malignancy

PRINCIPAL INVESTIGATOR: Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define the toxicities of the preparative regimen high dose Cytosan, etoposide, and carboplatin. To measure response rate in a group of patients with refractory solid tumors and CNS malignancies following this regimen and autologous bone marrow transplantation.

TECHNICAL APPROACH

Patients 21 years old or less will be entered in the study. After marrow is harvested and stored, ablative chemotherapy will be given for 5 days, followed by a day without chemotherapy. The next day, stored marrow will be reinfused as a "rescue" for the marrow damaged by the intensive therapy. This protocol accepts registrants who are refractory to other treatments for solid tumors and CNS tumors. Response will be evaluated at 60 days post marrow reinfusion.

PRIOR AND CURRENT PROGRESS

Three registrants have been entered in this protocol during the reporting year. Response at 60 days was two complete responses and one progressing disease. Toxicity has been mild. In November 1990, the protocol was revised to increase the total amount of carboplatin from 600 mg/m² to 1600 mg/m². This was requested in order to keep up with the current dose step in Phase I trials of this agent in children, and it was approved by the IRB on 27 Nov 90.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/23/91

WORK UNIT # 6267

DETAIL SUMMARY SHEET

TITLE: The Value of Sequential C-Reactive Protein Levels in Sickle Cell Anemia Patients Presenting with Symptoms of Crisis or Infection

KEYWORDS: sickle cell disease, c-reactive protein

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the clinical value of sequential c-reactive protein (CRP) levels in the differential diagnosis of bacterial infection vs. sickle crisis, and to compile data on age-related ranges of CRP values found in children with sickle cell anemia.

TECHNICAL APPROACH

CRP levels for baseline will be taken at time of regular checkups in the Outpatient Hematology Clinic, and updated every 6 months. At the time of presentation with symptoms of bacterial infection or sickle crisis, CRP values will be taken at set intervals and compared to the registrant's baseline. After the event is diagnosed by standard methods, differences in CRP values will then be analyzed.

PRIOR AND CURRENT PROGRESS

There have been 11 registrants to date. MAJ Moore has PCS'd to Fort Hood, TX, and a replacement investigator is being sought among the current fellows.

CONCLUSIONS

Study should remain open.

REPORT DATE: 06/12/91

WORK UNIT # 6268

DETAIL SUMMARY SHEET

TITLE: Retrospective Comparison of Neonatal Group B Streptococcal Bacteremia and Urine Latex Agglutination Testing

KEYWORDS: neonate, Group B Streptococcus, antigen

PRINCIPAL INVESTIGATOR: Ascher, David MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the sensitivity of the urine Group B Streptococcus (GBS) latex particle agglutination (LPA) assay under clinical conditions in a population of hospitalized newborns with culture confirmed GBS bacteremia.

TECHNICAL APPROACH

Retrospective chart review. Using STATISTIX 3.1, two-tailed Student's t-test will be used to compare mean differences for continuous variables between two groups, while the chi-square test for association will be used to compare proportional differences between two categorical variables.

PRIOR AND CURRENT PROGRESS

To date, 97 charts have been reviewed of neonates with culture confirmed GBS sepsis. The majority of data has been collected and analyzed. As new cases are identified, they are added to the data base. Several abstracts have been submitted, and a manuscript is being prepared for publication.

CONCLUSIONS

Overall, sensitivity of the urine GBS LPA assay, which included neonatal admissions for GBS bacteremia to six military medical centers over a 3 year period, was 52.9%. The sensitivity of the urine GBS LPA assay was lower than that previously reported and correlated with severity of disease. The urine GBS LPA assay in mildly ill newborns with GBS sepsis may be positive in less than 50% of cases, and a negative test does not rule out invasive GBS disease.

REPORT DATE: 08/15/91

WORK UNIT # 6273

DETAIL SUMMARY SHEET

TITLE: A Comparison of High Frequency Flow Interruption with High Frequency Jet Ventilation and Conventional Mechanical Ventilation in the Management of a Piglet Model of the Meconium Aspiration Syndrome

KEYWORDS: meconium, piglet, ventilation

PRINCIPAL INVESTIGATOR: Wiswell, Thomas LTC MC

ASSOCIATES: Foxter, Newton MAJ VC; Slayter, Michael LTC VS

DEPARTMENT: Department of Pediatrics

STATUS: Completed
APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 4,374 Previous FYs: \$ 0 Total: \$ 4,374

STUDY OBJECTIVE

To determine if ventilation with any of three types of high frequency ventilation offers any advantages compared with conventional mechanical ventilation in the Management of a Piglet Model of the Meconium Aspiration Syndrome.

TECHNICAL APPROACH

25% human meconium will be insufflated into the lungs of 56 newborn piglets. The animals will be randomized to ventilator management, with either conventional ventilation or one of three types of high frequency ventilation. Physiologic parameters will be followed and compared. Following 6 hours of ventilation, the animals will be euthanized. Lung sections will be taken and assessed by a pathologist blinded to individual animals' therapies. Scores will be given for the presence of four histologic parameters. The injury scores from animals managed with different types of ventilators will be compared.

PRIOR AND CURRENT PROGRESS

The laboratory portion of the data analysis portion have been completed. A manuscript has been written and is currently going through clearance for publication.

CONCLUSIONS

There are significantly more histopathologic alterations following conventional ventilation compared to any of the three types of high frequency ventilation. Our findings support further investigation into the utility of high frequency ventilation in the management of the meconium aspiration syndrome.

REPORT DATE: 03/12/91

WORK UNIT # 6121

DETAIL SUMMARY SHEET

TITLE: POG 7799 Rare Tumor Registry

KEYWORDS: rare tumors, tumors, pediatric tumors

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jan 1980

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To accumulate natural history data on malignancies which occur so rarely that larger series of cases cannot be accumulated at any single institution.

TECHNICAL APPROACH

Registry which contains pathology review of patients with rare tumors and annual reporting of status of patients.

PRIOR AND CURRENT PROGRESS

As of July 1990, there have been 248 cases reviewed and accepted into this registry. Thirty-one cases were submitted, reviewed, and found to be unacceptable. There are two cases that have been received, but not reviewed, and 10 cases submitted without slides.

CONCLUSIONS

Study should remain open.

REPORT DATE: 04/22/91

WORK UNIT # 6144

DETAIL SUMMARY SHEET

TITLE: POG 8158 NWTs Long Term Follow-up Study

KEYWORDS: Wilms' tumor, treatment complications

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Feb 1982

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To gather epidemiological and late effects data on Wilms' tumor patients.

TECHNICAL APPROACH

Data sent to coordinator to evaluate effects of the cancer and its treatment.

PRIOR AND CURRENT PROGRESS

In the reporting year, there were a total of 1,037 patients eligible for this study groupwide (22 eligible from WRAMC). There have been problems with completing the follow-up forms at the registering institutions, so an application for grant funding has been filed by the protocol coordinator to allow the data and statistical center to do the queries on patients whose follow-up has been transferred.

CONCLUSIONS

Study should remain open at WRAMC.

REPORT DATE: 07/31/91

WORK UNIT # 6148

DETAIL SUMMARY SHEET

TITLE: POG 8104 Comprehensive Care of the Child with Neuroblastoma: A Stage and Age Oriented Study, Phase III

KEYWORDS: neuroblastoma, Stage IV-S, cis-platinum

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: May 1982

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To prospectively evaluate the prognostic import of stage, using a pathological staging system, in children with neuroblastoma.

TECHNICAL APPROACH

Patients are treated with a variety of therapies according to their age and the stage of their disease.

PRIOR AND CURRENT PROGRESS

Study was closed to further accrual, as protocol 9047 has been activated. Four WRAMC registrants are alive at the time of this report. The POG study coordinators have not reported results for the past two meeting cycles and are expected to do so this October.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/06/91

WORK UNIT # 6162

DETAIL SUMMARY SHEET

TITLE: POG 8451 Intergroup Rhabdomyosarcoma III

KEYWORDS: rhabdomyosarcoma, cis-platinum, radiotherapy

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Dec 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To compare the effectiveness of various drug therapies in each clinical group, including the use of salvage chemotherapy, to evaluate prognostic factors; b) To determine if second and third look surgery will improve local disease control; and c) To attempt to devise a preoperative staging classification.

TECHNICAL APPROACH

Following complete surgical and medical staging and histologic subclassification, patients will be randomized to receive a specific chemo/radiation regimen, including salvage chemotherapy for advanced stages. Second and third look surgery will be used in some cases.

PRIOR AND CURRENT PROGRESS

There have been 1,072 patients registered groupwide. Most strata are closed for this protocol. Early analysis of response data for each stratum shows, in general, that the IRS III has been more successful. Response duration, overall, is better than results of the previous IRS. Toxicities reported continue to be mostly hematologic, and infectious complications remain a major concern. The one WRAMC registrant remains well; no new WRAMC registrants.

CONCLUSIONS

Study should remain open at WRAMC.

REPORT DATE: 05/16/91

WORK UNIT # 6166

DETAIL SUMMARY SHEET

TITLE: POG 8552 A Case-Control Study of Childhood Rhabdomyosarcoma

KEYWORDS: rhabdomyosarcoma, sarcoma, genetics

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the relationship between environmental exposures, gestational factors, and genetic factors and childhood rhabdomyosarcoma. To develop new methods for using subjects from collaborative cancer clinical trials for etiologic research.

TECHNICAL APPROACH

A telephone questionnaire (after consent is obtained) is undertaken for patients undergoing treatment on protocol and for a matched control group.

PRIOR AND CURRENT PROGRESS

This protocol was closed to patient accrual in May 1989 but remained open to report results. A total of 356 cases have been successfully interviewed. Interviews of matched controls have been completed for the final sample of 329 cases. Dr. Grufferman will be submitting three abstracts on the analysis of data collected on this study. The association of marijuana use in parents found in this study is consistent with the results from two other case control studies of recreational drug use by parents of children with other types of childhood cancer. An association between parent's cigarette smoking and childhood rhabdomyosarcoma that had been reported based on other studies was not found in the data collected and analyzed from POG 8552. Dr. Grufferman has also studied the limitations of using random digit telephone dialing for control selection in case-control epidemiology studies.

CONCLUSIONS

Study should be closed at WRAMC.

REPORT DATE: 03/12/91

WORK UNIT # 6175

DETAIL SUMMARY SHEET

TITLE: POG 8532 Treatment of Intracranial Ependymomas, A Pediatric Oncology Group Phase III Study

KEYWORDS: ependymomas, chemotherapy, tumors

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jan 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To estimate the occurrence of seeding of IVth ventricular ependymomas in the CNS after surgery and irradiation to study survival and relapse patterns.

TECHNICAL APPROACH

Careful testing to assess extent of disease after surgery (CT, myelogram, psychological testing, etc.). Testing is repeated after radiation and at 4 to 6 month intervals for 2 years.

PRIOR AND CURRENT PROGRESS

Groupwide, there have been 62 registrants; none are from WRAMC. Forty-three cases followed longer than 6 months are evaluable for this report. There are 37 progression-free survivors, 7 alive with disease, 4 are dead due to disease, and 1 is dead due to intercurrent disease. Preliminary review shows that the IVth ventricle/ependymoma stratum has had 5/8 without disease progression, all of whom have been followed longer than 2 years. CSF failures have only occurred on the IV/anaplastic stratum; one as an isolated event, and one with concurrent local failure. None of the IV/ependymoma cases have demonstrated CSF failure. There have been no unusual treatment-related toxicities due to the surgery and postoperative radiotherapy. One patient died of aspergillosis 1 month post-surgery.

CONCLUSIONS

Study has been closed to further accrual as of November 1990. Study should remain open at WRAMC for reporting on maturation of data for at least one more reporting year.

REPORT DATE: 07/08/91

WORK UNIT # 6176

DETAIL SUMMARY SHEET

TITLE: POG 8600 Laboratory Methods for POG 8600 ALinC 14 Classification (C)
Portion, Laboratory Manual, A Non-Therapeutic Study

KEYWORDS: lymphocytic leukemia, leukemia classification, ALL

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Completed
APPROVAL DATE: Apr 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine subgroup classification of acute lymphocytic leukemia (ALL) at the time of diagnosis using a variety of laboratory methods.

TECHNICAL APPROACH

Specimens of blood and/or bone marrow are sent to reference laboratories to accurately diagnose a child's leukemia.

PRIOR AND CURRENT PROGRESS

Protocol was closed in January 1991. Total enrollment was 2,784 (22 from WRAMC). This study is replaced by Work Unit #6278 (ALinC 15 Laboratory). This protocol is essentially a cell bank now. Currently, there are over 43 separate studies using material from the cell bank, and there have been over 30 publications resulting from studies that have used the POG 8600 material (no WRAMC studies or publications).

CONCLUSIONS

As there are no local projects planned, this protocol should be closed at WRAMC. Should registrants inquire about further study results, literature citations could be obtained from the study coordinators responsible for the cell bank.

REPORT DATE: 05/16/91

WORK UNIT # 6177

DETAIL SUMMARY SHEET

TITLE: POG 8602 Evaluation of Treatment Regimens in Acute Lymphoid Leukemia of Childhood (ALinC14), A POG Phase III Study

KEYWORDS: lymphocytic leukemia, childhood leukemia, methotrexate

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Edwards, E. Glenn MAJ MC; Blaney, Susan MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To treat patients with lymphocytic leukemia in order to provide optimal opportunity for possible cure.

TECHNICAL APPROACH

A comparison of regimens to determine if intermediate dose methotrexate (IDM) and ara-C in consolidation is superior to IDM + L-asparaginase, and if pulses of IDM/ara-C at 3 week intervals is superior to 12 week intervals.

PRIOR AND CURRENT PROGRESS

Protocol closed in January 1991, as accrual objectives had been met and the ALinC 15 studies were opened. Final accrual was 1,951 (18 from WRAMC). The overall induction complete response rate is about 97%. Early event-free survival analysis reveals no significant difference in any planned treatment question. Event-free survival at 3 years is about 78%. Isolated CNS, testicular, and marrow relapses are rare. Duke MY10 and St. Jude ploidy are significantly prognostic for early event-free survival. The major toxicity concerns for all regimens combined were infections, allergic reactions, transaminase elevation, and hematologic events. Of the 18 WRAMC patients, 8 are alive and off treatment, 3 are currently on therapy, 2 have relapsed, and 5 have died.

CONCLUSIONS

Study should remain open to report on WRAMC patients still on therapy.

REPORT DATE: 07/09/91

WORK UNIT # 6181

DETAIL SUMMARY SHEET

TITLE: POG 8625/8626 Combined Therapy and Restaging in the Treatment of Stages I, IIA, IIIA Hodgkin's Disease in Pediatric Patients, A Phase II Study

KEYWORDS: Hodgkin's disease, radiation, MOPP/ABVD

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Edwards, E. Glenn MAJ MC; Blaney, Susan MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jun 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To treat Hodgkin's disease in patients staged as I, IIA, and IIIA.

TECHNICAL APPROACH

Effectiveness and toxicities of three cycles of MOPP/ABVD are compared with two cycles of MOPP/ABVD plus radiation.

PRIOR AND CURRENT PROGRESS

There have been 152 registrants groupwide (4 from WRAMC). Overall, the response rate is 94%. Four patients have gone on to the standard dose radiation protocol (8626) for progressive/unresponsive disease. Size of mediastinal mass appears to be prognostic. Toxicity with MOPP-ABVD is mostly myelosuppressive, resulting in dose reductions and delays, as expected. Late effects are being compiled but at this time have not been compared to the late effects of Hodgkins' disease therapy on other protocols. There is still one WRAMC patient on therapy, two have completed therapy, and one patient did not respond and was treated on another protocol.

CONCLUSIONS

Study should remain open.

REPORT DATE: 09/26/91

WORK UNIT # 6182

DETAIL SUMMARY SHEET

TITLE: POG 8653/8654 A Study of Childhood Soft Tissue Sarcoma Other Than Rhabdomyosarcoma and Its Variants, A POG Phase III Study

KEYWORDS: soft tissue, synovial cell, sarcoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Completed
APPROVAL DATE: Jul 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To collect data on tissue sarcomas other than rhabdomyosarcoma and Ewing's, and b) To treat with surgery, chemotherapy, and radiation.

TECHNICAL APPROACH

Comparison of VACA to VACAD (VACA plus DTIC) chemotherapy regimens via randomization (protocol 8654).

PRIOR AND CURRENT PROGRESS

There have been 114 patients registered on the 8653/54 study. For good prognosis clinical groups, 28 were assigned to the chemotherapy (VACA) arm. Toxicity in this group has been tolerable and as expected. Disease-free survival during the first year is 83.7% and 81% during the second year. For poor prognosis patients, 24 have been assigned to the VACA arm, 20 to the VACA plus DTIC. Both complete and partial responses are being seen. Toxicity has been tolerable and as expected. Survival for poor prognosis patients is 60% in the first year and about 48% in the second and third. POG protocol was amended in September to temporarily close the VACA + DTIC arm, as there is a shortage of the drug DTIC. This will be presented at the October 1991 IRB meeting.

CONCLUSIONS

Study data will be reported on Work Unit #6184 (with an addendum submitted at this time for IRB approval). This protocol is being closed.

REPORT DATE: 08/14/91

WORK UNIT # 6184

DETAIL SUMMARY SHEET

TITLE: POG 8653 Study of Childhood Soft Tissue Sarcomas Other than Rhabdomyosarcoma and Its Variants, A POG Phase III Study

KEYWORDS: soft tissue sarcoma, synovial cell sarcoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: Aug 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To collect data on tissue sarcomas other than rhabdomyosarcoma and Ewing's; and b) To treat with surgery, chemotherapy, and radiation.

TECHNICAL APPROACH

To use adjuvant chemotherapy with vincristine, Adriamycin, cyclophosphamide, and actinomycin D (VACA) after surgery with or without postoperative radiation (POG 8653).

PRIOR AND CURRENT PROGRESS

There have been 70 registrants groupwide (none from WRAMC). Out of 29 registrants evaluable for response at this time, there are 7 complete, 1 partial, and 5 no responses for clinical group III disease. For clinical group IV disease, there have been 2 complete, 2 partial, 3 marginal, and 9 no responses seen. Disease-free survival for clinical group III is 65% during the first 3 years after therapy. Survival for this group is 75% during the first year and 60% during the second and third years. For clinical group IV, disease-free survival is 41.7% during the first year and 27.8% during the second. For the same time period and clinical group, survival is 47% and 38.2%. Toxicity is mostly hematologic and is acceptable.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/05/91

WORK UNIT # 6188

DETAIL SUMMARY SHEET

TITLE: POG 8650 National Wilm's Tumor Study - 4; A POG Phase III Study

KEYWORDS: Wilms' tumor, renal tumor, nephroblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Oct 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To gather data on morphology and correlate it with treatment and clinical outcome; and b) To refine clinical trials to reduce therapy to simpler and shorter regimens.

TECHNICAL APPROACH

To attempt to give the usual 5-day course on one day (has been done with other tumors) and to examine in randomized trial with current therapies.

PRIOR AND CURRENT PROGRESS

There are 1,191 patients on this study groupwide. Eight WRAMC patients have completed therapy and are alive and disease-free. One WRAMC registrant is on therapy and doing well. Response data so far does not show a statistically significant difference between the pulse intensive arm and the standard treatment arm. There is no new toxicity data to report. Changes in the protocol in the reporting year dealt with supportive treatment for patients receiving whole lung radiation therapy (antibiotic coverage to prevent *Pneumocystis carinii* pneumonitis). Investigators were also reminded to attempt to biopsy if lung metastasis is detected on CT. Last year's toxicity data has resulted in two published articles.

CONCLUSIONS

Study should remain open. Accrual is expected to be completed in 1994.

DETAIL SUMMARY SHEET

TITLE: POG 8616 Intensive Chemotherapies for Stage III Diffuse
Undifferentiated Lymphoma (DU NHL Burkitt and Non-Burkitt), A
Randomized Phase III Study

KEYWORDS: lymphoma, diffuse, undifferentiated

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jan 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To achieve chemotherapeutic cure in a majority of patients with Stage III DU-NHL; b) To compare two regimens for efficacy and toxicity; and c) To study correlation between treatment/response and LDH.

TECHNICAL APPROACH

Registrants must be 21 years old or less, previously untreated, and Stage III. Randomization is at diagnosis, between "Total B" regimen and a high dose Cytosan/methotrexate regimen.

PRIOR AND CURRENT PROGRESS

There have been 98 registrants groupwide; four are from WRAMC. Two WRAMC patients are in remission, one died early in the treatment from tumor lysis syndrome, and one died of a disease-related complication. Comparison of response between treatment arms remains masked. Overall, the complete response rate is 80%, complete response with provisions is 8%, and no response is 12%. Disease-free survival at one year is 66%, with no failures recorded after 12 months. Most relapses are local. As expected, severe hematologic toxicity is common, with hospital admissions for fever and neutropenia. Histologic review reports most patients on study are Burkitts or Undifferentiated NOS.

CONCLUSIONS

Study should remain open.

REPORT DATE: 04/11/91

WORK UNIT # 6192

DETAIL SUMMARY SHEET

TITLE: POG 8651 Osteosarcoma Study 2: A Randomized Trial of Pre-Surgical Chemotherapy Vs. Immediate Surgery and Adjuvant Chemotherapy in the Treatment of Non-Metastatic Osteosarcoma, A POG Phase III Study

KEYWORDS: osteosarcoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jan 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine whether pre-surgical chemotherapy will improve survival of subjects with non-metastatic osteosarcoma of the extremity or resectable bone compared to up-front surgery; b) To determine the impact of this approach on limb-sparing procedures; c) To evaluate the relationship of pre-surgery response with prognosis; and d) To study the tumor DNA content as a prognostic factor.

TECHNICAL APPROACH

Eligibility includes age less than 30 years, time less than 3 weeks from diagnosis, no prior history of cancer, and no prior therapy. The tumor must be biopsy-proven high-grade, resectable, and non-metastatic. Chemotherapy includes high-dose methotrexate, Adriamycin, cis-platinum, bleomycin, Cytosan, and actinomycin D. Pre-surgical chemotherapy randomization lasts 7 weeks.

PRIOR AND CURRENT PROGRESS

Groupwide there have been 76 registrants. Response and treatment specific results remain masked. Toxicities are as expected -- the most significant being neutropenia, stomatitis/mucositis, and transaminases. Disease-free survival for both treatment arms combined is 83% at 1 year and 64.8% at 1-2 years. Disease-free survival at 2-3 years remains at 64.8%; however, the curve is less stable (statistically, Standard Error is 22.2 for the 2-3 year data). There were no new WRAMC registrants in the reporting year. The WRAMC registrant is alive and disease-free.

CONCLUSIONS

Study should remain open.

DETAIL SUMMARY SHEET

TITLE: POG 8615 A Phase III Study of Large Cell Lymphomas in Children and Adolescents, A Comparison of Two Treatment Regimens, ACOP+ Vs. APO

KEYWORDS: lymphoma, large cell

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Feb 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine the influence of Cytosan therapy in advanced-stage large cell lymphomas in children and adolescents by comparing in a randomized prospective study the efficacy and toxicity of the above two modified regimens; b) To study these two regimens without adjuvant XRT and with only 12 months of therapy; and c) To study the clinical and biological characteristics of these large cell lymphomas.

TECHNICAL APPROACH

Children less than 21 years old with histologically confirmed large cell lymphomas of Murphy Stage III and IV are eligible. Randomization is at the start of therapy. Modified ACOP+ uses a vincristine/Cytosan/Adriamycin/prednisone induction, followed by 1 year of multiagent maintenance therapy. Modified APO has a similar induction minus Cytosan and a similar 12 month maintenance. Both arms are given IT MTX.

PRIOR AND CURRENT PROGRESS

There are 68 patients eligible for evaluation at this point (one from WRAMC). Comparison between treatment arms remains masked. The response rate for both arms is 93%. Toxicities are mostly hematologic, as expected. Due to the concerns about long-term cardiotoxicity from Adriamycin, the protocol was amended in August 1990 to substitute methotrexate after the total Adriamycin dose reaches 300 mg/M2. The WRAMC registrant completed therapy in March and has had a complete response.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/06/91

WORK UNIT # 6194

DETAIL SUMMARY SHEET

TITLE: POG 8617/8618 Therapy for B-Cell Acute Lymphoblastic Leukemia and Advanced Diffuse Undifferentiated Lymphomas, A Phase II Study

KEYWORDS: B-cell leukemia, lymphoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Feb 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To estimate CR rate and disease-free survival in patients with Stage IV diffuse undifferentiated (DU) NHL and B-ALL; and b) To estimate reinduction rate and DFS for patients in relapse with NHL.

TECHNICAL APPROACH

For POG 8617, children with untreated B-ALL, Stage IV DU-NHL, or diffuse lymphoma, non-lymphoblastic histology, in first relapse are eligible. For POG 8618, CNS relapse for NHL with non-lymphoblastic NHL, and isolated CNS relapse of 8617 registrants. Regimen involves initial vincristine/Cytosar/Adriamycin with intrathecal chemo, followed by IV MTX-ara-C. Thio-Tepa is substituted for IT MTX-ara-C on 8618. The consolidation phase uses the same regimen in three more courses.

PRIOR AND CURRENT PROGRESS

There have been a total of 87 registrants on this study (none from WRAMC). This study remains open for patients with newly diagnosed B-ALL and Stage IV diffuse undifferentiated NHL. The results for these groups have been extremely promising, while results from the closed stratum (relapsed patients) has been poor. Response rates to induction therapy are 86% for B-ALL, 90% for the DU NHL, and 45% for the relapsed group. Event-free survival is also promising for the first two strata. Repeated, profound myelosuppression is universal with this protocol, frequently accompanied by stomatitis, esophagitis and bacteremia. Clinical effects on immune function may persist for months after completion of therapy. No further neurotoxicities have been reported this year, suggesting that the dose intensity of Ara-C (amended October 1989) was the major basis for this problem.

CONCLUSIONS

Study should remain open until predecessor study is opened for accrual.

REPORT DATE: 07/10/91

WORK UNIT # 6195

DETAIL SUMMARY SHEET

TITLE: POG 8633/8634 The Treatment of Children Less Than Three Years of Age with Malignant Brain Tumors Using Postoperative Chemotherapy and Delayed Irradiation, A POG Phase II Study

KEYWORDS: medulloblastoma, brain irradiation, infant brain tumor

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Edwards, E. Glenn MAJ MC; Blaney, Susan MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine if postoperative chemotherapy in children less than 3 years old with brain tumors will allow delay of cranial irradiation; and b) To assess the response and toxicity rates.

TECHNICAL APPROACH

After surgery, infants are given four drugs over 2 months. If a good response occurs, this is continued for 2 years and then radiation is given. If there is not a complete response, radiation is given earlier.

PRIOR AND CURRENT PROGRESS

As reported last year, POG 8634 was closed to further accrual. Final registrations groupwide was 206 (4 from WRAMC). Of the 206 registrants, 48% (96) progressed prior to radiation and 61% (60) were registered on POG 8634 for radiation therapy. Response to 8634 has been seen in both strata; however, the majority of response data are not yet available for analysis, pending central review.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/13/91

WORK UNIT # 6196

DETAIL SUMMARY SHEET

TITLE: POG 8741/8742 Treatment of Stage D Neuroblastoma in Children Greater than 365 Days at Diagnosis, A POG Phase II/III Study

KEYWORDS: neuroblastoma, ifosfamide, metastatic neuroblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Phase II: To evaluate response rates in poor prognosis neuroblastoma with Phase II chemotherapy prior to conventional therapy.

Phase III: To evaluate the effectiveness of two chemotherapy regimens in a randomized trial; cisplatin/etoposide/cyclophosphamide/Adriamycin vs. high-dose cisplatin/etoposide/cyclophosphamide/Adriamycin. Data will also be collected to review the effect that tumor resectability has on remission rate and duration.

TECHNICAL APPROACH

Phase II: Cycles of Phase II drugs will be given to evaluate their potential use against neuroblastoma. The first drug is ifosfamide. The response will be evaluated, then conventional chemotherapy will be given.

Phase III: Newly diagnosed patients 365 days old and older who were treated on POG 8741 (Phase II) and failed, or newly diagnosed patients (Stage C and D) who have received no Phase II therapy, are treated with combination chemotherapy and, when possible, surgical removal of tumor.

PRIOR AND CURRENT PROGRESS

Phase II (POG 8741): Induction: initial and secondary samples are completed. Response rates (complete, partial and mixed) were 63% for ifosfamide, 61% for CBDCA, and 52% for CHIP. Epirubicin did not show adequate response and did not go beyond initial sampling.

Phase III (POG 8742): The Stage C stratum has 24 registrants (no other data reported yet). There are 208 Stage D patients groupwide; 137 are evaluable at this time. Treatment-specific response is masked -- arms combined; 51% are in CR, 26% in PR, and 12% in MR. Survival rates (post randomization) are 66% the 1st year, 38% the 2nd year, and 12% the 3rd year. Toxicity remains acceptable and is mostly hematologic. WRAMC has registered six patients; two have died, two transferred to Brooke Army Medical Center, one has completed therapy (partial response), and one progressed while on therapy and is receiving other treatment.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/16/91

WORK UNIT # 6197

DETAIL SUMMARY SHEET

TITLE: POG 8638: Randomized Phase II Study of Carboplatin Vs. CHIP in the Treatment of Children with Progressive or Recurrent Brain Tumors

KEYWORDS: brain tumors, platinum

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Completed
APPROVAL DATE: May 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine the effectiveness of carboplatin (CBDCA) and CHIP in the treatment of children with progressive or recurrent brain tumors; and b) To compare the toxicities associated with each agent.

TECHNICAL APPROACH

Children less than 21 years of age at initial diagnosis with recurrent or progressive brain tumors are eligible if not previously on more than one Phase II new agent study and have had no previous treatments with either drug. Patients are randomized to CHIP or CBDCA and receive two courses followed by evaluation for response. Chemotherapy is continued for 3-4 weeks if response occurs.

PRIOR AND CURRENT PROGRESS

This study was closed in April 1990, having met accrual objectives. The observed response rate was low, and there does not seem to be a difference between response seen on this protocol and the predecessor study (POG 8464: Carboplatin for Progressive CNS Tumors). Comparing CHIP to carboplatin, the difference in response is not significantly different either. The toxicity of both arms was statistically the same as well.

CONCLUSIONS

Study should be closed at WRAMC.

REPORT DATE: 05/16/91

WORK UNIT # 6198

DETAIL SUMMARY SHEET

TITLE: POG 8743: Treatment in "Better Risk" Neuroblastoma, POG Stage B (All Ages), And POG Stage C,D, and DS (IVS) Less Than 365 Days, A POG Phase III Study

KEYWORDS: neuroblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To identify patients who fail to achieve CR with Cytosan/Adriamycin and delayed surgery; b) To alter therapy in patients using CDDP & VM-26, and to evaluate their CR/survival rate; c) To evaluate survival in "better risk" and Stage IV-S patients, when randomized between observe only and CYC/ADR chemo; and d) To evaluate the prognostic value of LDH, N-MYC, NSE, and serum ferritin obtained at diagnosis.

TECHNICAL APPROACH

The patients eligible are all Stage B, less than 21 years, and Stage C, D, or DS (IVS), less than 365 days. Subjects with recurrent disease, Stage A and Stage DS less than 365 days, are also eligible. The above lab parameters are mandatory. All patients receive one course of Cytosan/Adriamycin, followed by continued induction depending on age and on tumor mitotic index.

PRIOR AND CURRENT PROGRESS

The study was closed October 1990, with a final accrual of 204 (one from WRAMC). Results so far suggest that therapy on this protocol is effective for hyperdiploid infants with Stages B, C, and D, or infants with Stage DS, or Stage B (over 1 year old). The response rate for the poorest prognostic group on this study is about 35% complete response, 41% partial response, and 24% no response/progressive disease. While this is better than results on this group from POG 8104, the study coordinators report that these results must be interpreted cautiously. Two year survival for the poorest prognostic group is 46%. For the hyperdiploid group mentioned above, the survival rate is 93%, for the Stage DS group - 89% and for the stage B group - 86%. Hematologic toxicities were the most common complication of therapy on this protocol.

CONCLUSIONS

Study should be closed.

REPORT DATE: 07/09/91

WORK UNIT # 6199

DETAIL SUMMARY SHEET

TITLE: POG 8704: T-Cell #3 Protocol, A POG Phase III Study

KEYWORDS: leukemia, T-cell

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine a) the efficacy of a multi-agent regimen against childhood T-cell leukemia and advanced T-cell lymphoma, b) the advantage gained with addition of high-dose asparaginase to the regimen, and c) the biology of these diseases.

TECHNICAL APPROACH

Children aged 12 months to 21 years are eligible. Simultaneous registration occurs on POG 8600 (leukemia classification protocol). No prior therapy is allowed. The lymphoma must be advanced stage. Pathology review required. Treatment was randomized to yes or no L-asp during maintenance, which lasts 90 weeks. CNS irradiation occurs for high white counts and CNS disease.

PRIOR AND CURRENT PROGRESS

As of November 1990, a total of 404 patients have been resistered (four from WRAMC). Induction remission rates remain at 97% (T-ALL) and 96% (T-NHL). Event-free survival figures at this time are 80.8% (T-ALL) and 84.1% (T-NHL) during years 1-2, and 66.8% (T-ALL) and 75.6% (T-NHL) during years 2-3. Toxicity is as expected. Preliminary review does not show either stage or white count to be significantly prognostic. Two WRAMC patients are still on therapy, one (previously reported) died on therapy of disease complications, and one registrant was disqualified as that registrant's disease pathology was re-classified as non-lymphocytic.

CONCLUSIONS

Study should remain open.

DETAIL SUMMARY SHEET

TITLE: POG 8631: Medulloblastoma Favorable Prognosis: Randomized Study of Reduced Dose Irradiation to Brain and Spinal Contents Vs. Standard Dose Irradiation, A POG Phase III Study in Conjunction with CCSG

KEYWORDS: medulloblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Completed
APPROVAL DATE: Jun 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine patterns of recurrence, disease-free survival, and survival; and b) To prospectively evaluate CNS functions of patients with favorable prognosis medulloblastoma given standard versus reduced dose radiotherapy.

TECHNICAL APPROACH

Children aged 3 to 21 years with diagnosed medulloblastoma are eligible. Total or almost total resection must have been accomplished, and no dissemination beyond the posterior fossa documented. No prior chemotherapy. Registrants on either arm will receive 5400 R to posterior fossa, but cerebrum and spine will receive either a standard 3600 R or reduced 2340 R.

PRIOR AND CURRENT PROGRESS

Entry to this study was suspended by the Joint POG and CCSG Committee in November 1990 for interim data analysis (per protocol specifications). The study was formally closed in January 1991 with the concurrence of the NCI, as statistically significant differences in response between the two treatment arms had been found. Study coordinators discussed appropriate management of the patients who had been treated on the lower dose radiation arm (with a poorer response rate) and have recommended surveillance only, as there is no evidence that adding further radiation or chemotherapy would be effective. There were no WRAMC registrants on this protocol.

CONCLUSIONS

Study should be closed at WRAMC.

REPORT DATE: 08/23/91

WORK UNIT # 6202

DETAIL SUMMARY SHEET

TITLE: POG 8739: Evaluation of Alpha Interferon in the Treatment of Recurrent Brain Tumors in Children, A POG Phase II Study

KEYWORDS: interferon (IFN), brain tumors

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of alpha-interferon (<-IFN) in children with brain tumors resistant to standard therapy in regard to response rate with different histologic subtypes and duration of response to <-IFN.

TECHNICAL APPROACH

Registrants are less than 21 years old with measurable tumors, and have not received chemotherapy in the preceding 2 weeks or radiation therapy in the preceding 3 months. Ten mega units of <-IFN are given IV 5 days/week for 4 weeks, and if responsive, subjects receive subsequent 4 week courses. Evaluation of response is at 4 weeks, or every other subsequent course.

PRIOR AND CURRENT PROGRESS

There have been 30 registrants in this study groupwide. Only the medulloblastoma stratum remains open; all others closed in May 1990 due others insufficient accrual. Response and toxicity are masked (Phase II trial). Toxicity has been mild. There were only two severe side effects in 21 patients whose toxicity data was evaluable. These were elevated transaminase levels and leukopenia. There are no WRAMC registrants.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/26/91

WORK UNIT # 6204

DETAIL SUMMARY SHEET

TITLE: POG 8751: Low Dose Methotrexate in the Treatment of Rhabdomyosarcoma, A
POG Phase II Study

KEYWORDS: methotrexate (MTX), rhabdomyosarcoma, POG

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jul 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine a) the response rate and duration of response in children with rhabdomyosarcoma treated with low-dose methotrexate (LD MTX) given every 6 hours for 6 doses, and b) the type and duration of toxicity of low dose sustained oral methotrexate.

TECHNICAL APPROACH

This is a single armed Phase II study of children with biopsy-proven rhabdomyosarcoma unresponsive to standard therapy. Patients cannot have had previous exposure to MTX. MTX is given orally every 6 hours for six to eight doses per course and designed to sustain MTX levels of 0.5 micromolar for more than 36 hours per pulse.

PRIOR AND CURRENT PROGRESS

Twenty-eight patients have been entered in this study (none from WRAMC). Twelve were randomized to the MTX + leucovorin; 16 to the MTX alone arm. Toxicity data is available for 26 patients: 12 patients completed 31 evaluable courses without leucovorin, and 14 patients completed 47 evaluable courses with leucovorin. Toxicity was mostly hematologic, as expected (worse in the group who did not receive leucovorin).

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/14/91

WORK UNIT # 6205

DETAIL SUMMARY SHEET

TITLE: POG 8759: The Effectiveness of Phase II Agents in Untreated Metastatic Osteosarcoma or Unresectable Primary Osteosarcoma Vs. Previously Treated Recurrent Osteosarcoma, POG Phase II/III Study

KEYWORDS: osteosarcoma, recurrent, primary

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Aug 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To study the response rate to ifosfamide in newly diagnosed metastatic unresectable osteosarcoma or in osteosarcoma presenting as a second malignancy and to study the addition of the agent to a standard treatment regimen for effectiveness and toxicity; and b) To gain biologic information about the tumor.

TECHNICAL APPROACH

Eligible new patients (biopsy proven) will be treated with two courses of ifosfamide upfront, evaluated for response (including biopsy and a surgical excision), and then continued on standard chemotherapy and ifosfamide. Those registrants having recurrence will continue, if responsive, on ifosfamide only.

PRIOR AND CURRENT PROGRESS

Study was closed in October 1990 as accrual objectives were completed. Study coordinators report that stratum 1 (metastatic at presentation) has 36 registrants; 32 are evaluable for response; 1 complete, 9 partial, 3 mixed, 10 stable, 9 no response/progressive disease. Disease-free survival is 60% during first year, 45% during second year. Survival for this stratum is 71.3% (first year) and 56.7% (second year). The one WRAMC registrant was on this stratum and has completed therapy, with a complete response. Therapy has been relatively well tolerated, with no changes in the treatment plan due to excessive toxicity. The other two stratum were not reported by the coordinators. They plan to report that data in October 1991.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/12/91

WORK UNIT # 6206

DETAIL SUMMARY SHEET

TITLE: POG 8763: Evaluation of Response and Toxicity of Ifosfamide and VP-16-213 in Children with Resistant Malignant Tumors, A POG Phase II Study

KEYWORDS: solid tumors, ifosfamide/VP-16

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Aug 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the antitumor activity and toxicity of ifosfamide (IFX) plus VP-16 against a spectrum of childhood malignant solid tumors resistant to conventional chemotherapy.

TECHNICAL APPROACH

Registrants must be less than 21 years, with confirmed and measurable solid tumor, and be off therapy. VP-16 and IFX are given in 3 day courses, 3 weeks apart, for 18 months if response occurs.

PRIOR AND CURRENT PROGRESS

This study was closed to accrual in August 1990. During the past year, no data was reported by the study coordinators. A report will be included in the October 1991 Bi-Annual Report. The WRAMC patient who had stable disease on study remains stable off study.

CONCLUSIONS

Study should remain open for one more year to report data when released by study coordinators.

REPORT DATE: 09/18/91

WORK UNIT # 6207

DETAIL SUMMARY SHEET

TITLE: POG 8719: Trial of Shortened Therapy without Maintenance for the Treatment of Localized Non-Hodgkin's Lymphoma, A POG Phase III Study

KEYWORDS: non-Hodgkin's lymphoma, localized

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To compare the survival and disease-free survival in patients receiving 9 weeks of induction/consolidation versus patients receiving similar 9 weeks + 24 weeks of maintenance; and b) To continue cancer biopsy studies of POG #8315.

TECHNICAL APPROACH

Children under 21 years with no prior therapy are eligible. Induction/consolidation therapy is with Cytosan/Adriamycin/vincristine and prednisone, with intrathecal medications for head and neck primaries only. Maintenance therapy uses oral 6MP/MTX.

PRIOR AND CURRENT PROGRESS

There have been two WRAMC registrants since this protocol was activated (one transferred, the other has completed therapy and is in remission). Groupwide, there have been 170 registrants; 139 are eligible for analysis of response at this time. The complete remission rate is 94%. Disease-free survival is 87% through the end of the second year, and 82% in the third year post-treatment. Toxicity has been acceptable, mostly hematologic. This protocol has had rapid accrual and may close eight months ahead of schedule.

CONCLUSIONS

Study should remain open.

REPORT DATE: 09/18/91

WORK UNIT # 6209

DETAIL SUMMARY SHEET

TITLE: POG 8726: Alpha-Interferon in Histiocytosis X and Other Non-Malignant Histiocytic Disease, A POG Phase II Study

KEYWORDS: histiocytosis X, interferon

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine a) the disease-free response of patients with histiocytosis X (HX) and related diseases to treatment with alpha-interferon (<-IFN), and b) the toxicities of <-IFN in children with HX and related diseases.

TECHNICAL APPROACH

Registrants must be less than 21 years of age with biopsy-proven recurrent HX after conventional therapy with one or more boney lesions, or recurrent HX variants. No concurrent chemotherapy in prior <-IFN.

PRIOR AND CURRENT PROGRESS

This study was closed to further accrual in 1989. The one WRAMC registrant completed therapy in late August 1990 and received a bone marrow transplant that September. This registrant is the only patient who responded out of 10. In the past two meeting cycles, the principal investigator has not reported on this study.

CONCLUSIONS

Study should be closed.

REPORT DATE: 09/18/91

WORK UNIT # 6210

DETAIL SUMMARY SHEET

TITLE: POG 8761: A Phase II Study of Homoharringtonine for the Treatment of Children with Refractory Nonlymphoblastic Leukemia

KEYWORDS: non-lymphoblastic, leukemia, homoharringtonine

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Sep 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the efficacy of homoharringtonine (HHT) for the therapy of refractory acute non-lymphoblastic leukemia (ANLL) in children, and further assess the toxicity of HHT.

TECHNICAL APPROACH

Registrants must be a) less than 21 years; b) in relapse, with recovery from prior therapy; c) with no current therapy; and d) with no CNS disease. Treatment is 10 day continuous IV courses, given every 21 days.

PRIOR AND CURRENT PROGRESS

There have been no WRAMC registrants. Groupwide, as of this report, there have been 17 registrants. Response data is masked; toxicity is reported.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/05/91

WORK UNIT # 6211

DETAIL SUMMARY SHEET

TITLE: POG 8731: A Phase II Study of Low-Dose "Continuous" Oral Methotrexate
in the Treatment of Children with Progressive or Recurrent Brain Tumors

KEYWORDS: methotrexate, brain tumors

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the effectiveness of this regimen and evaluate toxicity.

TECHNICAL APPROACH

Eligibility criteria include age less than 21-years-old with recurrent or progressive brain tumor, no more than one previous phase II agent for treatment, and measurable residual tumor.

PRIOR AND CURRENT PROGRESS

A total of 70 patients have been registered as of the last POG report. Accrual for the medullablastoma stratum has been completed. Response data for that stratum indicates that out of eight evaluable registrants, there were three whose disease stabilized, two who had no response, and six who had progressive disease. Response for other strata is masked. Toxicities are as expected, with the most common causes of delay in therapy being stomatitis, thrombocytopenia, and increased liver function tests.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/05/91

WORK UNIT # 6212

DETAIL SUMMARY SHEET

TITLE: POG 8764: Chemotherapy Regimen for Early and Initial Induction
Failures in Childhood Acute Lymphoblastic Leukemia, A POG Phase II
Study

KEYWORDS: leukemia, lymphoblastic

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Oct 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To use a continuous infusion ara-C/VM-26 induction regimen to assess remission rate and one year DFS; and b) To use CDNA and oncogene probes for characterizing the unique subpopulation.

TECHNICAL APPROACH

Eligible patients must have residual disease following conventional induction therapy or have relapsed within 6 weeks after initial remission induction.

PRIOR AND CURRENT PROGRESS

As of August 1990, there have been 20 patients accrued. This accrual rate at 6.9 per year is less than projected (10). Response and disease-free survival are masked. Reported induction toxicities have mostly been hematologic (anemia, thrombocytopenia, and neutropenia). Out of 15 patients evaluable for toxicity, there have been 13 reported infectious episodes during induction. To date, there have been no WRAMC registrants on this study.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/07/91

WORK UNIT # 6213

DETAIL SUMMARY SHEET

TITLE: POG 8823/24: Recombinant Alpha Interferon in Childhood Chronic Myelogenous Leukemia, Phase II

KEYWORDS: leukemia, chronic myloid, interferon

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Hastings, Constance MD

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: Dec 1987

FUNDING: Current FY: \$ 3,720 Previous FYs: \$ 8,241 Total: \$ 11,961

STUDY OBJECTIVE

To determine a) toxicity, rate and duration of response to therapy with recombinant alpha-interferon (<-IFN) for newly diagnosed "adult" CML and for "juvenile" CML occurring within the first two decades of life; b) obtain prospective clinical, laboratory, and genetic data on cases of ACML and JCML treated with recombinant <-IFN.

TECHNICAL APPROACH

Qualified registrants must be 21 years of age or less, with no previous treatment, except for emergency lowering of tumor burden. All subjects must meet appropriate specific physical and laboratory eligibility criteria for AMCL or JMCL. Monitoring of biologic markers will be performed at several reference labs, including WRAMC Department of Pediatrics lab (serum IFN, B12, LAP, fetal Hb, and muramidase). Patient cells will be separated and cryopreserved at WRAMC and marrow morphology reviewed. IFN will be given as IV daily for 14-day induction, followed by a subcutaneous IFN injection three times a week for maintenance therapy for a minimum of 18 months, according to response.

PRIOR AND CURRENT PROGRESS

Groupwide accrual is at 30 registrants (none from WRAMC). Response and survival data remain masked. There have been no study amendments in the reporting year. Toxicity continues to be acceptable and manageable with IFN dose manipulation. Through December 1990, the WRAMC laboratory had a total of 323 specimens stored (64 from 1988-89, the first year of the study).

CONCLUSIONS

Study should remain open, and an increase in specimen processing and storage is expected (increase in registrants and time on study for existing registrants).

REPORT DATE: 05/15/91

WORK UNIT # 6214

DETAIL SUMMARY SHEET

TITLE: POG 8696/97: Treatment of Hepatoblastoma (HB) with Surgery,
Chemotherapy, and Radiation Therapy

KEYWORDS: hepatoblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Apr 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To obtain data on natural disease course in completely resected, favorable histology hepatoblastoma (HB) with surgery alone; and b) To evaluate toxicity of and response to DDP + VCR + 5-FU used in conjunction with surgery and for those with residual disease, with the addition of radiation therapy.

TECHNICAL APPROACH

Patients 21 years of age or younger diagnosed with HB, previously untreated except by surgery (entry within 4 weeks post-surgery). POG 8696 is Stage I disease, which is observed after surgery, and POG 8797 is for disease that has advanced and includes induction therapy (DDP x 2 weeks, DDP + VCR + 5-FU x 5) and radiation therapy for more advanced disease.

PRIOR AND CURRENT PROGRESS

This study closed to patient accrual in October 1989 and has been replaced by POG 8945. There have been no registrants from WRAMC. Groupwide, accrual and evaluability were very good; 62 registrants will be evaluable for survival, and 40 are now evaluable for response. There have been 26 complete responses, 9 partial responses, and 5 had disease progression. Forty of 54 evaluable patients who did not have metastatic disease (74%) are alive (median survival - 36 months), and 41 out of 46 patients who achieved a complete response (89%) have survived with the same median (36 months). Most patients have had severe hematologic toxicity after at least one of the courses of chemotherapy. One patient had severe electrolyte problems.

CONCLUSIONS

Study should be closed at WRAMC as there are no WRAMC registrants, and the subsequent study (8945) is open for accrual.

REPORT DATE: 04/09/91

WORK UNIT # 6216

DETAIL SUMMARY SHEET

TITLE: POG 8710: Protocol for Second Induction and Maintenance in Childhood Acute Lymphoblastic Leukemia (SIMAL #5), A POG Phase III Study

KEYWORDS: lymphoblastic leukemia

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To compare disease free survival (DFS) of regimen including MTX/VM-26 with a control; b) To compare DFS of regimen including IFN with a control; c) To estimate and compare remission duration and toxicity in patients receiving either MTX/VM-26 or IFN as continuous therapy components; d) To determine prognostic value of clinical and biological features at relapse, including immunophenotyping and cytogenetics, all patients; IFN receptors and oncogene profile, INF patients.

TECHNICAL APPROACH

Patients are 21 years or younger and diagnosed with non-T, non-B acute lymphoblastic or undifferentiated leukemia on initial classification or non-Hodgkin's lymphoma with first marrow relapse (more than 25% blasts), first hematologic relapse, or first overt extramedullary relapse (CNS disease excluded) while receiving chemotherapy, or within 6 months of stopping therapy. Patients are not eligible for higher priority protocol. Induction is given over 4 weeks (PBDA/TTT); then patient's treatment is randomized between the three arms described in the above objective.

PRIOR AND CURRENT PROGRESS

Study was closed due to sufficient accrual in May 1991. At last report, there were 277 registrants (none from WRAMC). The complete response rate is 73.7%, partial response rate is 5.5% and no response rate is 16.6%. Toxicity is as expected (mostly hematologic). Disease-free survival is 39.9% at 0-6 months, 25.6% at 6-12 months, and 22.9% at 12-18 months. Arm-specific comparisons remain masked. There have been no new WRAMC patients.

CONCLUSIONS

Study should remain open to report unmasked data in upcoming year.

REPORT DATE: 05/15/91

WORK UNIT # 6217

DETAIL SUMMARY SHEET

TITLE: POG 8725: Randomized Study of Intensive Chemotherapy (MOPP/ABVD Plus/Minus Low Dose Total Nodal Radiation Therapy in the Treatment of Stages IIB, IIIA2, IIIB, IV Hodgkin's Disease in Pediatric Patients, Phase III

KEYWORDS: Hodgkin's disease, nodal radiation, MOPP/ABVD

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine in a randomized study whether the addition of low dose total nodal irradiation to four courses of MOPP/ABVD combination chemotherapy will improve the duration of complete remission and survival when compared with patients who have had chemotherapy only.

TECHNICAL APPROACH

Patients are 21 years old and younger who have previously untreated, histologically proven Hodgkin's disease (Stage IIB, IIIA2, IIIB, and IV).

PRIOR AND CURRENT PROGRESS

There have been 114 patients registered groupwide (four from WRAMC). At the completion of chemotherapy, 61 out of 68 registrants had a complete response (89%). Six had evidence of disease, one patient with suspected disease refused biopsy and went on to receive radiation therapy. Hematologic toxicity with related infections were the most common toxicities of chemotherapy. Twenty-seven registrants received radiation therapy; 14 registrants completed XRT without complications. At two years, survival is at about 88%.

CONCLUSIONS

Study should remain open.

REPORT DATE: 09/18/91

WORK UNIT # 6221

DETAIL SUMMARY SHEET

TITLE: POG 8821: Intensive Multiagent Therapy Vs. Autologous Bone Marrow Transplant Early in First CR for Children with Acute Myelocytic Leukemia - A Phase III Study

KEYWORDS: autologous bone marrow, transplant, acute myelocytic leukemia

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine DFS with intensive chemotherapy using non-cross resistant drug pairs; b) To determine if short-term intensive therapy with autologous bone marrow transplant (with 4-Hydroperoxycyclophosphamide purge) is effective therapy; and c) To compare the two regimens' results and to correlate outcome with clinical and laboratory features.

TECHNICAL APPROACH

Registrants are 21 years of age and younger with previously untreated acute myelocytic leukemia (AML). Induction for both arms uses intrathecal ara-C, daunomycin, ara-C, 6-TB, followed by high dose ara-C. Patients are then randomized to receive either IT ara-C, VP-16/5-AZA plus ABMT with 4-HC purge, or IT ara-C, HDAC/daunomycin, ara-C/6-TG, VP-16/5-AZA.

PRIOR AND CURRENT PROGRESS

There have been no new WRAMC registrants in 1991. The WRAMC registrants from 1990 have both completed therapy and are in complete remission. Groupwide, accrual totals 319 registrants. Response for 277 evaluable registrants is 86% remission and for registrants with extramedullary disease, 70.6%. Duration of response drops to 55% by the beginning of the second year and stays the same through the third year. As expected for this protocol, toxicity is considerable but has been acceptable to date. The consent form was revised in August to include long-term toxicity of WP-16 (increased risk of secondary AML) that has recently been reported. Other amendments during 1990 were the addition of Busulfan pharmacokinetics studies for registrants less than 5 years later.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/06/91

WORK UNIT # 6224

DETAIL SUMMARY SHEET

TITLE: POG 8827: Treatment of Children with Hodgkin's Disease in Relapse, A
POG Phase II Study

KEYWORDS: Hodgkin's disease, childhood, chemotherapy

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate overall effectiveness of cytosine arabinoside, cis-platin, and VP-16 in children with Hodgkin's disease in relapse.

TECHNICAL APPROACH

Patients are under 21 years of age at diagnosis and have failed MOPP/ABVD or equivalent treatment. Hodgkin's disease must have progressed beyond consideration that radiation alone might be curative. Separate ara-C, cisplatin, and VP-16 bolus, with IV infusion of ara-C in between. One cycle takes 12 hours, with a total of three administrations per cycle. This is repeated every 4 weeks for a total of eight cycles, with the option to add two cycles for patients who obtain a CR or PR late in therapy. Radiation therapy following CR or PR is offered on this protocol.

PRIOR AND CURRENT PROGRESS

There have been 19 registrants groupwide; none are from WRAMC. Response is masked at this time. Toxicities for the 19 patients so far have been mostly hematologic (neutropenia, thrombocytopenia).

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/12/91

WORK UNIT # 6227

DETAIL SUMMARY SHEET

TITLE: POG 8862: Treatment of First Marrow and/or Extramedullary Relapse of Childhood Acute T-Lymphoblastic Leukemia and T-Non-Hodgkin's Lymphoma with Combination Chemotherapy Including 2'-Deoxycoformycin

KEYWORDS: first relapse, T-lymphoblastic leukemia, T-non-Hodgkin's lymphoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess toxicity and efficacy of low dose 2'-deoxycoformycin (DCF) in prolonging the duration of second remission of T-ALL/T-NHL. To correlate clinical response and toxicities with plasma levels of the metabolized forms of DCF and the in vitro sensitivity of leukemia cells to the drug.

TECHNICAL APPROACH

Patients 21 years old and less in first relapse of T-ALL/T-NHL are treated with an induction regimen of daunorubicin, vincristine, prednisone, and L-asparaginase. Continuation therapy is IV methotrexate and 6-MP, and registrants are randomized to arms receiving this continuation therapy with or without IV push DCF. Triple intrathecal drugs are given throughout the entire regimen.

PRIOR AND CURRENT PROGRESS

There have been 42 patients registered groupwide; none are from WRAMC. The major efficacy analysis is restricted to marrow-involved patients. The complete response rate is 66.7%, partial response is 15.4%, and no response is 15.4%. Early deaths accounted for the remaining 2.5% of the registrants in this analysis. Overall event free survival for 39 evaluable registrants is 44.1% at 0-3 months, 23.4% at 3-6 months, 15.6% at 6-12 months. Toxicities remain mostly hematologic, as expected. In November 1990, the study was opened to testicular relapse patients, as this stratum was closed on POG 8304.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/12/91

WORK UNIT # 6228

DETAIL SUMMARY SHEET

TITLE: POG 8866: Polyethylene Glycol-Conjugated L-Asparaginase Vs. Native L-Asparaginase in Combination with Standard Agents as Second Line Induction Therapy for Children with Acute Lymphocytic Leukemia in Bone Marrow Relapse, Phase II Randomized Trial

KEYWORDS: PEG L-asparaginase, relapsed ALL, children

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare in a randomized trial, the efficacy, toxicity, and feasibility of administration of PEG L-asparaginase (L-asp) to native L-asp as part of chemotherapy for ALL in second relapse. To determine serum half-life and duration.

TECHNICAL APPROACH

Patients 21 years old and younger with ALL in second marrow relapse are randomized to receive induction therapy with either PEG L-asp or with native L-asp, along with vincristine and prednisone.

PRIOR AND CURRENT PROGRESS

There have been 44 patients registered on this study groupwide; none are from WRAMC. There is no new report from POG concerning response or disease-free survival. Treatment group specific toxicity remains masked. Liver toxicity (SGOT, SGPT, and bilirubin), coagulation factors, and drug fever are the most commonly reported toxicities.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/12/91

WORK UNIT # 6229

DETAIL SUMMARY SHEET

TITLE: POG 8850: Evaluation of Vincristine, Adriamycin, Cyclophosphamide and Dactinomycin with or without the Addition of Ifosfamide and Etoposide in the Rx of Patients with Newly Diagnosed Ewing's Sarcoma of Primitive Neuroectodermal Tumor or Bone, Phase III

KEYWORDS: Ewing's sarcoma, primitive neuroectodermal, childhood tumor

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare treatment effectiveness of etoposide and ifosfamide added to the standard treatment regimen. To assess toxicity and adverse orthopedic outcome associated with disease and therapies employed. To assess potential significance of tumor characteristics in prognosis.

TECHNICAL APPROACH

Patients aged 30 or less will be randomized to receive the standard chemotherapy (vincristine, Adriamycin, and cyclophosphamide) or the standard along with ifosfamide and etoposide.

PRIOR AND CURRENT PROGRESS

There have been 72 patients registered groupwide; none are from WRAMC. Response is masked. Therapy is generally well tolerated, neutropenia being the most common severe toxicity.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/12/91

WORK UNIT # 6230

DETAIL SUMMARY SHEET

TITLE: POG 8832: Pre-irradiation Combination Chemotherapy with Cisplatin and Ara-C for Children with Incompletely Resected Supratentorial Malignant Tumors: A Phase II Study

KEYWORDS: cisplatin, Ara-C, supratentorial malignancy

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine toxicities of cis-platin and Ara-C given before cranial irradiation. To estimate efficacy of 15 weeks of therapy with this chemotherapy, and to establish the feasibility and completeness of second surgical resection for incompletely-resected supratentorial tumors after this initial chemotherapy.

TECHNICAL APPROACH

Patients between 3 and 21 years of age will receive 15 weeks of combination chemotherapy after initial surgical resection, followed by second surgery (if needed), 6 weeks of radiation therapy.

PRIOR AND CURRENT PROGRESS

Groupwide, there have been 52 registrants; none from WRAMC. Response remains masked. The glial neoplasm stratum has closed due to completion of accrual goals. Neutropenia with infectious complications, thrombocytopenia, and auditory problems remain the most significant side effects.

CONCLUSIONS

Study should remain open to allow accrual on remaining strata.

REPORT DATE: 05/06/91

WORK UNIT # 6232

DETAIL SUMMARY SHEET

TITLE: POG 8833 Pre-Radiation Chemotherapy in the Treatment of Children with Brain Stem Tumors, Phase II

KEYWORDS: brain stem tumors, chemotherapy, childhood

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) To evaluate response of children with brain stem gliomas to four cycles of HD cyclophosphamide and cis-platinum (response to be measured by CT/MRI and neurological exams). 2) To monitor acute and chronic toxicities of chemotherapy and unusual XRT-related toxicity. 3) To estimate post-therapy control of disease for patients on study.

TECHNICAL APPROACH

Patients over 3 years of age and less than 21 years, with diagnosis of glioma arising in the pons. Chemotherapy is delivered over the first 13 weeks on study (four cycles), followed by 110 cGy/fraction bid 5 days/week for 6 weeks.

PRIOR AND CURRENT PROGRESS

As reported last year, this study has been closed to further accrual. A total of 32 registrants are evaluable at this time. Response to chemotherapy is as follows: 3 partial responses, 2 marginal responses; 20 registrants had stable disease, 6 had progressive disease, and 1 registrant had a marginal response before disease progression. Of the 20 children with stable disease, 7 improved neurologically. Response to radiotherapy is as follows: 11 patients were not evaluable, 4 had partial responses, 10 had stable disease, 3 responded marginally, and 4 had disease progression. Four patients are alive, one with evidence of disease progression (28 registrants died between 1-22 months after starting therapy). Comparison of survival results with POG 8495 (hyperfractionated radiotherapy without chemotherapy) does not show a significant difference in survival outcome.

CONCLUSIONS

Study should be closed.

REPORT DATE: 05/06/91

WORK UNIT # 6233

DETAIL SUMMARY SHEET

TITLE: POG 8820 VP-16, AMS, and 5-Azacytidine in Refractory ANLL, Phase II-III Study

KEYWORDS: ANLL, refractory disease, chemotherapy

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) To compare, in a randomized trial, remission rates of VP-16/AMSA vs. VP-16/AMSA and Az in refractory or recurrent acute nonlymphocytic leukemia (ANLL). 2) To determine duration of remission using pulses of induction regimen as continuation therapy. 3) To study the relative toxicities of the two regimens.

TECHNICAL APPROACH

Pediatric patients who have failed induction or relapsed on frontline therapy. Induction is 5 days of AMSA, with 3 days of VP-16 (concurrent). Induction is two cycles; a third may be given if patient responds. Maintenance therapy is this therapy repeated at 4 week intervals. Az regimen includes this drug for 2 days of the cycle.

PRIOR AND CURRENT PROGRESS

There have been 76 registrants on this study as of February 1991 (no new WRAMC registrants). The complete response rate is about 30%. Early toxicity data indicate a substantial proportion (46 out of 66 patients) have at least grade 3 infections with this regimen. There have been no additional cases of fatal sepsis since the last report.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6236

DETAIL SUMMARY SHEET

TITLE: POG 8829 A Protocol for a Case Control Study of Hodgkin's Disease in Childhood

KEYWORDS: childhood, Hodgkin's disease, epidemiology

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: McFarland, Janetta MAJ AN; Blaney, Susan MAJ MC

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To collect specific data on the epidemiology of childhood Hodgkin's disease (HD). Parameters to be examined are: possible variance between adult and childhood forms of HD, patterns of previous infectious disease exposure, socioeconomic patterns, familial aggregation, and risk for other diseases. b) To evaluate the parameters listed above according to histologic subtype, stage, and age at diagnosis.

TECHNICAL APPROACH

Newly diagnosed HD patients, ages 15 years and less, seen at POG institutions will complete (the parents will complete) a questionnaire by phone, donate serum for future evaluation, and have clinical study data evaluated. Matched controls will be identified and interviewed over the telephone.

PRIOR AND CURRENT PROGRESS

There have been 269 potentially eligible cases registered (six from WRAMC). There have been 93 interviews with registrants completed; 61 pending. Twenty control group participants have also been interviewed.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6237

DETAIL SUMMARY SHEET

TITLE: POG 8398 Up Front Alternating Chemotherapy for Acute Lymphocytic Leukemia: A Pilot Study

KEYWORDS: infant, ALL

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the toxicity of alternating chemotherapy pairs in acute lymphocytic leukemia (ALL): 6-mercaptopurine/methotrexate, VM-26/cytosine arabinoside, daunomycin/cytosine arabinoside. To obtain preliminary data about disease-free survival and to determine feasibility.

TECHNICAL APPROACH

POG 8600 registrants who have high risk ALL, without prior therapy, and less than one year old are eligible. Chemotherapy listed above is given.

PRIOR AND CURRENT PROGRESS

Study has accrued 118 registrants (none from WRAMC) and was closed in early 1991, as the successor study (AlinC 15) opened. Overall, the induction complete response rate is 92%. Toxicity has been manageable (mostly hematologic). The VM-26/cytosine arabinoside was the most hematologically toxic of the drug combinations. Event-free survival for infants this past 12 months makes this therapy much less promising than previously reported results. Event-free survival for children over 1 year old has been the highest among the confirmed pre-B group. At 3-6 years, it is about 64%. For the non-T, non-pre-B group, event-free survival is about 33% at 3-6 years. Infants have an event-free survival of about 34% during the first year, dropping to about 29% in the second year.

CONCLUSIONS

Study should be closed at WRAC.

REPORT DATE: 05/16/91

WORK UNIT # 6238

DETAIL SUMMARY SHEET

TITLE: POG 8889 Intergroup Rhabdomyosarcoma Study-IV: Pilot Study for
Clinical Group IV Disease

KEYWORDS: rhabdomyosarcoma, chemotherapy

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine feasibility/toxicity of ifosfamide and doxorubicin (ID) as induction chemotherapy and, subsequently, in combination with vincristine, actinomycin-D, and cyclophosphamide (VAC) as maintenance chemotherapy, to treat rhabdomyosarcoma and its variants. This regimen is to be piloted for its possible incorporation into the three-arm IRS-IV study to follow.

TECHNICAL APPROACH

Patients, ages 21 years and younger, with no prior treatment of clinical group IV rhabdomyosarcoma, extraosseous Ewing's, or undifferentiated sarcoma will be given the chemotherapy described above.

PRIOR AND CURRENT PROGRESS

There have been 104 patients registered on this study (none from WRAMC). The overall response rate is 71%. Data on the amount of time until complete response is achieved appears similar to what was observed on the Intergroup Rhabdomyosarcoma Study (IRS) pilots for IRS-II and for IRS-III. This suggests there is no disadvantage to withholding VAC until week 12 and radiation therapy until week 18. Severe myelosuppression occurred in 82% of the 84 evaluable registrants. Twenty of those registrants had infectious complications related to the myelosuppression (there were two deaths due to sepsis). A third death occurred that was possibly related to pulmonary toxicity and radiation-induced complications. However, toxicity was as expected for this regimen, and therapy on this protocol has not been revised.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6242

DETAIL SUMMARY SHEET

TITLE: POG 8828 Late Effects of Treatment of Hodgkin's Disease: A POG
Nontherapeutic Study

KEYWORDS: childhood, Hodgkin's disease, long-term effects

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To estimate incidence of late effects following treatment for Hodgkin's disease on current frontline POG studies (8625, 8725) and to attempt to identify pre-treatment and/or on-treatment factors which predict high risk of specific late effects.

TECHNICAL APPROACH

Registrants are patients on POG 8625 or 8725 and are followed through completion of late effects study forms every three years.

PRIOR AND CURRENT PROGRESS

There have been 135 patients registered on this study (seven from WRAMC). Study coordinators report that the projected accrual will probably not be met; however, the study still has the potential to yield important data on the late effects of Hodgkin's disease and its treatment. There have been no amendments to the protocol this reporting year.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6243

DETAIL SUMMARY SHEET

TITLE: POG 8863 High Dose Cytosine Arabinoside in the Treatment of Advanced Childhood Tumors Resistant to Conventional Therapy, Phase II

KEYWORDS: recurrent/refractory, solid tumors, cytosine arabinoside

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine efficacy and toxicity of various advanced refractory solid tumors to high-dose ara-C (HDAC).

TECHNICAL APPROACH

Patients are 21 years and younger at diagnosis with biopsy-proven, measurable, malignant solid tumor, life expectancy greater than six weeks, adequate nutritional status, blood counts, renal and hepatic function, and no previous HDAC. HDAC is given over 3 days, with about 3 weeks in between cycles.

PRIOR AND CURRENT PROGRESS

There have been 27 patients registered groupwide (none from WRAMC). Twenty-four are eligible for this study. Response remains masked. Fourteen registrants have had one course of chemotherapy, seven have had two courses, and one patient has received four courses. Toxicity was mostly myelosuppression, which may have been exacerbated by lower than normal bone marrow reserves due to prior chemotherapy and radiation. There were no drug-related deaths.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6244

DETAIL SUMMARY SHEET

TITLE: POG 8865 Recombinant Alpha Interferon in Relapsed T-Cell Disease: A Phase II Study

KEYWORDS: interferon, T-cell, malignancy

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess response rate of T-cell malignancy to alpha-IFN (<-IFN) who have failed standard therapy. To correlate response rate to presence of IFN receptors, oncogene receptors, modulation of oncogene expression, modulation of oncogene expression by IFN, DNA content, and antiproliferative effect of IFN in-vitro on T-cell lymphoblasts.

TECHNICAL APPROACH

Patients 21 years and younger with refractory T-cell disease in second marrow relapse, meeting entry requirements concerning previous therapy, and with no evidence of serious uncontrolled infection are eligible for this study. Induction of triple intrathecal methotrexate, high-dose cytoxan, and ara-C is given and continued with pulse maintenance therapy. Induction IFN is given for 5 days x 2 weeks, followed by 3 x week maintenance course.

PRIOR AND CURRENT PROGRESS

There have been 16 patients registered groupwide as of February 1991. There have not been any registrants from WRAMC. Response is masked. The most common toxicities have been infections, nausea/vomiting, transaminase elevations, diarrhea, and decreased coagulation factors.

CONCLUSIONS

Study should remain open.

REPORT DATE: 06/09/91

WORK UNIT # 6248

DETAIL SUMMARY SHEET

TITLE: POG 8495: Hyperfractionation in Brain Stem Gliomas in Children, Phase I

KEYWORDS: hyperfractionated XRT, brain stem glioma, children

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Completed

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess feasibility and response in patients with brain stem gliomas treated with hyperfractionated radiation therapy, to study the immediate and late side effects of this therapy, and to test the feasibility of dose escalation in this group of patients.

TECHNICAL APPROACH

Phase I study of patients between 3 and 21 years of age with brain stem gliomas who meet diagnostic criteria and have not had previous radiation or chemotherapy.

PRIOR AND CURRENT PROGRESS

This study was closed to further accrual in July 1990, as a sufficient number of patients had been registered (136; 4 not included for evaluation with the rest of study data). Response for the 7560 cGy dose level is pending review. Overall survival for the three dose groups is not significantly different. As expected, the degree of toxicity increased with the dose level.

CONCLUSIONS

Study should be closed at WRAMC, as there are no patients being followed on this study.

REPORT DATE: 07/09/91

WORK UNIT # 6249

DETAIL SUMMARY SHEET

TITLE: POG 8788: Intergroup Rhabdomyosarcoma Study IV: A Pilot Study for
Clinical Group III Disease

KEYWORDS: childhood, rhabdomyosarcoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Jun 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Pilot study comparing feasibility and toxicity of vincristine/Adriamycin/cytosine (VAC), or vincristine/Adriamycin/ifosfamide (VAI), or vincristine/ifosfamide/VP-16 (VIE) used with hyperfractionated radiation therapy.

TECHNICAL APPROACH

Patients at least 21 years old, with clinical group III RMS or extraosseous Ewing's sarcoma, are assigned a treatment regimen according to the institution's assigned regimen (WRAMC uses VAI) randomized between the above mentioned three-drug regimens. Favorable histology head/neck or genitourinary tumors that would be eligible for IRS III are ineligible for this study, as are patients who had prior radiation or chemotherapy. Induction therapy is 16 weeks of chemotherapy and radiation, with continuation therapy of 20-99 weeks of chemotherapy.

PRIOR AND CURRENT PROGRESS

There are a total of 220 registrants groupwide (none from WRAMC). Response rates at this time are slightly lower than reported last year. The most common toxicities are myelosuppression and mucositis. Amendments in 1990 include the closing of the VAI regimen (sufficient accrual) and a dose increase in cyclophosphamide on the VAC regimen. The VAI and VIE regimens were also revised so that ifosfamide therapy does not extend beyond 52 weeks, as the incidence of nephro-toxicity increases after 1 year of ifosfamide therapy. Due to the nature of the study (cytotoxic therapy given to a large number of patients), toxicity information is provided in a report from the cooperative oncology group and is available through the principal investigator listed above.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/26/91

WORK UNIT # 6250

DETAIL SUMMARY SHEET

TITLE: POG 8935 A Study of Biological Behavior of Optic Pathway Tumors

KEYWORDS: optic pathway tumors, children, biology

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To assess time to progression in patients with optic pathway tumors (OPT) and with or without neurofibromatosis; b) To estimate response at 2 years post-radiation therapy; c) To estimate incidence of progression in patients with neurofibromatosis; d) To assess long-term effects of being treated for OPT under the age of 21; and e) To assess the value of neurophysiologic techniques in the assessment of disease progression and response.

TECHNICAL APPROACH

Patients 21 years old and less with previously untreated OPT. If disease progresses when registrant is over 5 years old, either radiation therapy for 6 weeks or surgery with or without radiation therapy will be given. If registrant is 5 years old or less, carboplatin will be given on POG protocol 8936 (WU# 6251).

PRIOR AND CURRENT PROGRESS

As of November 1990, there have been 20 registrants groupwide (none from WRAMC). Of the 20, 9 were simultaneously registered on POG 8936 with progressive disease. Neurofibromatosis was diagnosed in 50% of the registrants. It is too early to report on the completion of other goals of this study.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/26/91

WORK UNIT # 6251

DETAIL SUMMARY SHEET

TITLE: POG 8936 Carboplatin in Progressive Optic Pathway Tumors: Phase II

KEYWORDS: carboplatin, optic pathway tumors, children

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess the response rate to carboplatin (CBDCA) in children with optic pathway tumors, and to assess the efficacy of CBDCA in delaying the progression of disease.

TECHNICAL APPROACH

Registrants on POG 8935 who are 5 years old or less, who have evidence of optic pathway tumor progression, are given IV CBDCA over 1 hour every 4 weeks for 18 months.

PRIOR AND CURRENT PROGRESS

There have been 10 registrants groupwide since this protocol opened (no WRAMC registrants). It is too early to report on response. Hematologic toxicity is the most common problem; however, this is as expected and is acceptable.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/05/91

WORK UNIT # 6252

DETAIL SUMMARY SHEET

TITLE: POG 8945 An Intergroup Protocol for the Treatment of Hepatoblastoma and Hepatocellular Carcinoma, Phase III

KEYWORDS: hepatoblastoma, hepatocellular carcinoma, children

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare response rates of hepatocellular carcinoma and hepatoblastoma in patients less than 21 years of age when treated with either Adriamycin and cisplatin or cisplatin/5-FU/vincristine. Also, to compare the event-free survival rate and toxicity of the two regimens. Serum alpha-fetoprotein levels will also be studied to determine their value as a relapse predictor. Pure fetal histology tumors are also to be studied.

TECHNICAL APPROACH

Patients less than 21 years old with hepatocellular carcinoma or incompletely resected, unfavorable histology hepatoblastoma are randomized to receive either cisplatin and Adriamycin or cisplatin/5-FU/vincristine. Response is evaluated and resection performed as indicated. Serial serum levels of alphafetoprotein and ferritin will be drawn, and their relationship to relapse will be analyzed. Favorable histology hepatoblastoma will be treated with Adriamycin and response evaluated.

PRIOR AND CURRENT PROGRESS

As of June 1990, there were 15 registrants groupwide (3 hepatoblastomas, 12 hepatocellular carcinomas). No unusual toxicity has been reported; it is too early for any other analysis. There have been no registrants from WRAMC in this reporting year.

CONCLUSIONS

Study should remain open. Analysis is not complete.

REPORT DATE: 03/05/91

WORK UNIT # 6253

DETAIL SUMMARY SHEET

TITLE: POG 8930 Comprehensive Genetic Analysis of Brain Tumors

KEYWORDS: brain tumors, children, genetics

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine clinical significance of cellular DNA content, the clinical implications of cytogenetic abnormalities at diagnosis, of amplification or re-arrangement of proto-oncogenes or allelic loss. To attempt to derive tumor cell lines and a bank of frozen tissue for further studies.

TECHNICAL APPROACH

Fresh tissue submitted for flow cytometry, cytogenetic studies, molecular studies, and cryopreservation, along with peripheral blood specimens, as pediatric brain tumor patients are registered on POG front-line therapeutic studies.

PRIOR AND CURRENT PROGRESS

Material on 25 brain tumor patients has been submitted; however, only five patients have been registered on POG front-line studies. While this may reflect the lack of available studies, correlation of cytogenetics and treatment outcome will be impaired if this accrual pattern continues. All new POG front-line studies will have data submission incorporated into treatment protocol guidelines. There were no registrants from WRAMC in the reporting year.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/06/91

WORK UNIT # 6260

DETAIL SUMMARY SHEET

TITLE: POG 9046 A Molecular Genetic Analysis of Wilms' Tumors and Nephrogenic Rests

KEYWORDS: Wilm's tumor, cytogenetics

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define patterns of cytogenetic changes in Wilms' tumor and associated nephrogenic rest tissue and to correlate these patterns with clinicopathologic findings. To establish a bank of molecularly and cytogenetically characterized Wilms' tumors with matched constitutional tissue (lymphoid cells from serum samples).

TECHNICAL APPROACH

Patients 16 years old or less with a previously untreated histologically proven Wilms' tumor of any histological subtype will submit fresh tumor tissue and blood samples for genetic analysis and banking.

PRIOR AND CURRENT PROGRESS

Since this study opened, material from 48 cases has been submitted. Correlation with clinicopathologic features has not yet been attempted. Material from two Wilms' tumor cases at WRAMC has been submitted for this study.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/06/91

WORK UNIT # 6261

DETAIL SUMMARY SHEET

TITLE: POG 9047 Neuroblastoma Biology Protocol

KEYWORDS: cytogenetics, neuroblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

SERVICE: Pediatric Oncology Group

STATUS: Ongoing

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To analyze cytogenetics of neuroblastoma cells and determine the clinical significance of genetic variations found, compared to conventional clinical, histologic, and biologic variables in predicting response to treatment or outcome. To develop a neuroblastoma serum and tissue bank for future studies, and to collect natural history and lab data on patients with untreated disease (stages A and DS).

TECHNICAL APPROACH

All newly-diagnosed patients 21 years old or less who are registered on POG neuroblastoma treatment protocols, or stage A or DS (favorable risk), will submit discarded biopsy material and serum for cytogenetic studies and banking.

PRIOR AND CURRENT PROGRESS

This study opened for registration in February 1990. There have been 24 patients entered on the study (none from WRAMC). It is too early to report results.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/07/91

WORK UNIT # 6263

DETAIL SUMMARY SHEET

TITLE: POG 9049 A Study of High Risk Malignant Germ Cell Tumors in Children: A Phase III Treatment Study

KEYWORDS: malignant germ cell tumor, children

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare the efficacy of two regimens: high-dose cisplatin or standard dose cisplatin used with the drugs etoposide and bleomycin. Data will also be gathered on the response at 12 weeks; organ toxicity (acute and long term), prognostic significance of tumor and metastatic tumor characteristics, significance of several tumor markers at different points in the course of treatment, and tumor and constitutional cytogenetics will be analyzed.

TECHNICAL APPROACH

Pediatric germ cell tumor patients ages 21 years or less with histologically verified disease will be randomized to receive chemotherapy following their surgery with either a regimen of high or standard dose cisplatin, plus etoposide and bleomycin.

PRIOR AND CURRENT PROGRESS

Nineteen patients have been registered on this intergroup study (POG and Children's Cancer Study Group). Accrual is at the projected rate. It is too early to report on response or disease-free survival. Toxicity has been as expected. There was one WRAMC patient registered this year. The patient completed therapy and is in remission.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6265

DETAIL SUMMARY SHEET

TITLE: POG 9082 Development of Intervention Strategies to Reduce the Time
between Symptom Onset and Diagnosis of Childhood Cancer

KEYWORDS: symptom onset, childhood cancer, diagnosis

PRINCIPAL INVESTIGATOR: Maybee, David COL MC
ASSOCIATES: McFarland, Janetta MAJ AN

DEPARTMENT: Department of Pediatrics
SERVICE: Pediatric Oncology Group

STATUS: Ongoing
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To describe constellation of symptoms that occur prior to definitive diagnosis of childhood cancer and to evaluate factors that may be associated with the length of time between symptom onset and diagnosis. To determine if these symptoms or time period until diagnosis influence prognosis independent of treatment and disease stage. To provide data that may be used to develop intervention strategies.

TECHNICAL APPROACH

All previously untreated pediatric oncology patients registered on POG treatment studies are registered on this protocol. Questionnaire is given to parents within 7 days of registration on treatment protocol.

PRIOR AND CURRENT PROGRESS

There have been 278 patients registered as of February 1991. Ten patients from WRAMC have been registered. It is too early to report any other study results.

CONCLUSIONS

Study should remain open.

REPORT DATE: 05/15/91

WORK UNIT # 6269

DETAIL SUMMARY SHEET

TITLE: POG 9060 Intensive QOD Ifosfamide for the Treatment of Children with Recurrent or Progressive CNS Tumors, Phase II

KEYWORDS: ifosfamide, recurrent brain tumor

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Blaney, Susan MAJ MC; Edwards, E. Glenn MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the activity of ifosfamide delivered QOD (i.e., M,W,F) in the treatment of children with recurrent/progressive CNS tumors, to evaluate toxicity of this regimen, especially neurotoxicity for patients with (1) prior cisplatin therapy, (2) no prior cisplatin with a total dose less than 300 mg/M2, and (3) prior cisplatin with a total dose greater than 300 mg/M2.

TECHNICAL APPROACH

Patients 21 years old and less with primary intracranial tumor are given ifosfamide three times a week every 21 days as long as the patient continues to demonstrate at least stable disease.

PRIOR AND CURRENT PROGRESS

As of December 1990, there have been 23 patients registered (none from WRAMC). Fourteen have completed at least one 3-day course of ifosfamide. There has been no severe neurotoxicity (grade 3 or 4). Two episodes of transient grade 2 neuro-toxicity was reported in two patients with prior cisplatin doses of less than 300 mg/M2. Hematologic recovery has been complete by day 22 (mean) with a range of 11-39 days. Two patients have had proven infections during their nadirs. Two patients have had hemorrhagic cystitis (one had prior cyclophosphamide). One patient had severe renal toxicity (Na = 113, 24 hours after first dose of ifosfamide). There were no amendments made to the protocol this reporting year.

CONCLUSIONS

Study should remain open.

REPORT DATE: 07/10/91

WORK UNIT # 6270

DETAIL SUMMARY SHEET

TITLE: POG 9048 The Treatment of Children with Localized Germ Cell Tumors,
Phase II

KEYWORDS: localized, malignant germ cell tumor, children

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Edwards, E. Glenn MAJ MC; Blaney, Susan MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine long-term, event free survival for better risk patients treated with surgery alone; to determine long-term, event free survival for poorer risk patients treated with cisplatin, etoposide, and bleomycin; and to determine prognostic significance of tumor histology, site, size, tumor cytogenetics, and constitutional sex chromosomes.

TECHNICAL APPROACH

Pediatric patients 21 years old and less with good risk malignant germ cell tumors are treated with surgery alone and observed for increase in tumor marker levels. If tumor markers rise, good risk patients are treated, as are the other tumor histologies eligible for this protocol, with four cycles of cisplatin, etoposide, and bleomycin. Tumor tissue cytogenetic studies are also done on all registrants.

PRIOR AND CURRENT PROGRESS

Since this study opened in May 1990, there have been eight patients registered from POG (none from WRAMC). It is too soon for any analysis.

CONCLUSIONS

Study should remain open.

REPORT DATE: 07/09/91

WORK UNIT # 6271

DETAIL SUMMARY SHEET

TITLE: POG 9061 The Treatment of Isolated Central Nervous System Leukemia

KEYWORDS: infant leukemia, CNS relapse

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

ASSOCIATES: Edwards, E. Glenn MAJ MC; Blaney, Susan MAJ MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the feasibility and toxicity of intensified systemic treatment with delayed craniospinal radiation for children with acute lymphoblastic leukemia (ALL) and isolated central nervous system (CNS) disease. To study the pharmacokinetics and cytotoxic effect within the cerebrospinal fluid (CSF) of intravenous 6-MP given as a single agent in an up-front treatment window.

TECHNICAL APPROACH

Children less than 1 year old and with ALL in first marrow remission with isolated CNS relapse are given intravenous 6-MP for 2 weeks before a second induction, consolidation, and intensification chemotherapy regimen, followed by craniospinal irradiation and a 76 week maintenance period.

PRIOR AND CURRENT PROGRESS

Accrual as of February 1991 is 13 patients (no WRAMC registrants). So far, complete clearing of leukemia cells in the CSF has not been achieved during the 6-MP window, so escalation of the infusion duration is continuing. At last report, all patients were less than 31 weeks into therapy, and one has completed CNS irradiation. Toxicities have been acceptable and are as expected for the chemotherapy regimen.

CONCLUSIONS

Study should remain open.

REPORT DATE: 08/08/91

WORK UNIT # 6272

DETAIL SUMMARY SHEET

TITLE: POG 9031 The Treatment of Children with High Stage Medulloblastoma:
Cisplatin/VP-16 Pre Vs. Post Irradiation, Phase III

KEYWORDS: cisplatin, radiotherapy, medulloblastoma

PRINCIPAL INVESTIGATOR: Maybee, David COL MC

DEPARTMENT: Department of Pediatrics

STATUS: Ongoing

SERVICE: Pediatric Oncology Group

APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare survival of children treated with and without pre-irradiation chemotherapy. To determine if c-myc gene amplification in medulloblastoma is associated with an adverse prognosis.

TECHNICAL APPROACH

Children between the ages of 3 and 21 years are randomized to receive either pre-irradiation chemotherapy with cisplatin and VP-16, followed by more cycles of chemotherapy or a second treatment; which is irradiation followed by chemotherapy with cisplatin and VP-16. Specimens are sent to a central office to determine c-myc amplification.

PRIOR AND CURRENT PROGRESS

At last report, there were 15 registrants groupwide (none from WRAMC). It is too soon to report on any of the data.

CONCLUSIONS

Study should remain open.

REPORT DATE: 03/05/91

WORK UNIT # 3600

DETAIL SUMMARY SHEET

TITLE: Determination of Noncompliance in Prescription Pickup

KEYWORDS: non-compliance, prescription

PRINCIPAL INVESTIGATOR: Nelson, Bruce LTC MS

ASSOCIATES: Buchanan, Terry MAJ MS

SERVICE: Pharmacy Service

STATUS: Ongoing

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the most common reasons why patients fail to pick up new and refill prescriptions from the Pharmacy. Secondly, to identify demographically, any significant differences between patients who pick up their prescriptions versus patients who fail to claim their prescriptions.

TECHNICAL APPROACH

Collect an unselected convenience sample of 200 patients with unclaimed new or refill prescriptions. After identifying patients, they will be contacted by phone, asked to participate in the study, and given a short telephone questionnaire. The second part of the study will attempt to identify significant demographic differences between patients who fail to pick up their medication and those who pick up their prescriptions. A random sample of 186 patients from both groups will be reviewed for differences. Data will be analyzed using logistic regression.

PRIOR AND CURRENT PROGRESS

Part one telephone surveys have been completed and some descriptive data have been analyzed. Part two of the study has been suspended due to significant staffing shortages in the Pharmacy, Operation Desert Shield/Storm, and other factors. It is hoped that the data collection for part two will be restarted soon.

CONCLUSIONS

No conclusions have been made.

REPORT DATE: 06/04/91

WORK UNIT # 3601

DETAIL SUMMARY SHEET

TITLE: Evaluation of the Effect of Clinical Pharmacists on Inpatient Health Care Outcomes

KEYWORDS: clinical pharmacist, intervention, mortality

PRINCIPAL INVESTIGATOR: Bjornson, Darrell LTC MS

ASSOCIATES: Hiner, William COL MS; Potyk, Roger LTC MS

SERVICE: Pharmacy Service

STATUS: Ongoing

APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To estimate the effect of clinical pharmacist intervention on patient length of stay, patient drug cost per admission, and mortality in the medical and surgical inpatient population.

TECHNICAL APPROACH

This will be an experimental study comparing patients followed by medical care teams with clinical pharmacists (two general medicine and one general surgery team) with concurrent, non-randomized control groups of patients who will be followed by medical care teams without clinical pharmacists (three general medicine and two general surgery teams). Three clinical pharmacists will be randomly assigned to each of two teams on the general medicine wards and one team on the general surgery ward. The clinical pharmacist in the Hematology/Oncology area will continue to function in that area and data on his patients will be compared with regional norms.

PRIOR AND CURRENT PROGRESS

The study began in October 1990 and will continue through January 1992. Presently 1,854 patients have been followed and have had data collected on them. It is anticipated that there will be approximately 3,000 patients in the study by January 1992. There have been two presentations on the study's progress to the American Society of Hospital Pharmacists (ASHP) Advisory Committee; one in December 1990, and one in April 1991. The methodology will be presented at the Federation of International Pharmacy Meeting (FIP) and the ASHP Clinical Midyear Meeting in September 1991 and December 1991. Final analysis and interpretation will be in the summer of 1992.

CONCLUSIONS

No conclusions can be drawn from the data at this time. Only descriptive information has been collected. Inferential statistics will be applied at the conclusion of the study.

REPORT DATE: 03/11/91

WORK UNIT # 9609

DETAIL SUMMARY SHEET

TITLE: Radial Nerve F Wave Study

KEYWORDS: F wave response, radial nerve, extensor indicus proprius

PRINCIPAL INVESTIGATOR: Bryant, Phillip MAJ MC

ASSOCIATES: Robinson, Michael CPT MC; Fujimoto, Ronald MAJ MC

SERVICE: Physical Medicine and Rehabilitation Svc

STATUS: Ongoing

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To obtain a normal latency value for the radial nerve F wave.

TECHNICAL APPROACH

A mean latency value (in milliseconds) will be determined for the F response of the extensor indicus proprius (EIP) muscle, innervated by the radial nerve. Values will be standardized by height. A technique of surface stimulation with cathode placement lateral to the biceps tendon at the flexion crease of the antecubital fossa and surface recording over the EIP muscle will be employed. A Disa 1500 electrodiagnostic machine will be used to provide the stimulation and recording of the F response.

PRIOR AND CURRENT PROGRESS

This study has been delayed by the departure of the previous principal investigator to another duty station. Radial F wave response studies were performed on 28 subjects, in most cases bilaterally. Analysis of the compiled data revealed that additional subjects were warranted to obtain statistical significance. Twenty-three further studies are planned. No serious or unexpected adverse reactions have occurred as a result of this study. Healthy subjects without peripheral neurological impairments have been evaluated. One person with bilateral brachial plexopathies has also been studied to exemplify the utility of the technique.

CONCLUSIONS

Pending statistical analysis of the results.

REPORT DATE: 03/11/91

WORK UNIT # 9611

DETAIL SUMMARY SHEET

TITLE: Normative Isokinetic Torque Values of Quadriceps and Hamstrings in Active Duty Military Subjects

KEYWORDS: isokinetic exercise, torque, biodex

PRINCIPAL INVESTIGATOR: Nowlin, Rebecca CPT SP

ASSOCIATES: Sutlive, Jacenta CPT SP; Sinnott, Melissa MAJ SP

SERVICE: Physical Medicine and Rehabilitation Svc

STATUS: Completed

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To establish a data base of normative values for hamstring and quadricep performance in male, active-duty Army soldiers, as measured by the Biodex B-2000.

TECHNICAL APPROACH

This study will involve 50 active duty male soldiers between the ages of 18 and 34. Each subject will be evaluated for possible knee injury and be given a consent form explaining the study. Leg dominance will be determined by having the subject kick a ball. Subjects will be randomly placed in different testing groups, either testing at a fast speed or low speed first and either testing the dominant or non-dominant limb first. An isokinetic strength evaluation will be performed at 60, 180, and 300 degrees/second for the quadriceps and hamstrings.

PRIOR AND CURRENT PROGRESS

All 50 subjects have been tested, and data analysis has been performed with the assistance of the DCI statisticians. Both Statistix and SPSS programs were used for the data analysis. A reliability study was also performed by testing five different subjects at four different points in time on the Biodex B-2000. This study indicated greater than a 90% reliability index for the unit. There have been no serious or unexpected adverse reactions, and none of the subjects have withdrawn. Patients will benefit from this information as clinicians try to interpret information obtained from the Biodex B-2000 evaluation.

CONCLUSIONS

When comparing the data obtained in this study to that reported by other authors using a different population, we found a slightly higher mean peak torque at all speeds. Our findings are consistent with other authors in reference to ratio of quadricep to hamstring strength and dominant to non-dominant strength.

REPORT DATE: 09/06/91

WORK UNIT # 1326-90

DETAIL SUMMARY SHEET

TITLE: Predictors of Thyroid Dysfunction in Patients Treated with Lithium

KEYWORDS: lithium, thyroid, predictors

PRINCIPAL INVESTIGATOR: Joslin, Scott CPT MC

ASSOCIATES: Burman, Kenneth COL MC; Wartofsky, Leonard COL MC

DEPARTMENT: Department of Psychiatry

STATUS: Ongoing
APPROVAL DATE: Sep 1990

FUNDING: Current FY: \$ 34 Previous FYs: \$ 0 Total: \$ 34

STUDY OBJECTIVE

To prospectively determine the incidence of anatomical or functional thyroid disease in patients treated with lithium (Li) over the course of 1 year. To determine what factors by history, biochemical status, autoimmune status, and functional status may predict the course of dysfunction over the course of one year. To evaluate changes in iodine content of the thyroid in Li patients.

TECHNICAL APPROACH

Evaluation of 100 patients who are being treated for the first time with Li with thyroid function testing, TSI, TBII, physical examination, ultrasound, fluorescent iodine scanning and serial Li level analysis at the initiation of Li treatment, and again after 2 months, 6 months, and 1 year.

PRIOR AND CURRENT PROGRESS

The fluorescent iodine scanner has been made operational and the support staff within the Department of Psychiatry have been briefed and will participate in assisting with enrollment. The loss of a room to perform the fluorescent iodine scans is being remedied. Patient enrollment should begin in approximately 30 days.

CONCLUSIONS

None, to date.

REPORT DATE: 08/06/91

WORK UNIT # 7239

DETAIL SUMMARY SHEET

TITLE: Visual Information Processing in Psychiatric Patients

KEYWORDS: vision, acuity, schizophrenia

PRINCIPAL INVESTIGATOR: Blair, Sidney CAPT MC

DEPARTMENT: Department of Psychiatry

STATUS: Ongoing

APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare vernier visual acuity in normal subjects and in psychiatric patients.

TECHNICAL APPROACH

Subjects attempt to discriminate computer-generated vernier stimuli. Responses are tallied and analyzed by computer.

PRIOR AND CURRENT PROGRESS

Prior work in this study showed that our visual stimulus parameters acuity results comparable to those of other investigators and that an auditory stimulus presented after the visual stimulus increased the latency of response but did not change vernier acuity. Current work studied interaction of auditory and visual stimulus preceeding or following the visual stimulus, in increments of 50 ms, up to a maximum of 300 ms. Over this range there was no change in visual acuity. Sixteen subjects have been studied. This work was carried on in collaboration with Work Unit #7244.

CONCLUSIONS

Auditory and visual stimuli interact even in normal subjects. In the range of stimuli explored thus far, with the auditory stimulus either preceeding or following the visual stimulus by up to 300 ms, the interaction results in increased latency of response but not in degraded visual acuity.

REPORT DATE: 04/18/91

WORK UNIT # 7240

DETAIL SUMMARY SHEET

TITLE: Cerebral Dysfunction in Schizophrenic Subtypes

KEYWORDS: schizophrenia, neuropsychology, electrophysiology

PRINCIPAL INVESTIGATOR: Warden, Debra MD

ASSOCIATES: Anderson, Milton CPT MC; Coats, Michael MD

DEPARTMENT: Department of Psychiatry

STATUS: Ongoing
APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if clinically identified subtypes of schizophrenic patients exhibit findings on neuropsychological and neurophysiological testing consistent with predominantly left hemisphere, right hemisphere, or bilateral frontal lobe dysfunction.

TECHNICAL APPROACH

To identify positive and negative symptom patients by a Positive and Negative Symptom Scale (PANSS) after a semistructured interview. The Schedule for Affective Disorders and Schizophrenia (SADS) will be utilized to confirm the diagnosis of schizophrenia, according to Research Diagnostic Criteria (RDC). Patients will then receive Evoked Potential testing, EEG with brainmapping, neuropsychological testing, and neurological exam.

PRIOR AND CURRENT PROGRESS

A substantial amount of time was spent familiarizing researchers with the specific instruments (PANNS, SADS, RDC) in order to assure interrater reliability and validity. Eight patients and no controls have entered the protocol to date. One patient withdrew, citing stress involved in protocol due to additional hospital appointments. She has been followed closely by her psychiatrist with no adverse effects. This protocol does not directly benefit patients, though three patients have stated their satisfaction at being able to potentially help others through a study of the illness.

CONCLUSIONS

Deferred.

REPORT DATE: 07/12/91

WORK UNIT # 7241

DETAIL SUMMARY SHEET

TITLE: The Relationship Between Hypnotic Capacity and Dissociative Experience

KEYWORDS: hypnosis, dissociation

PRINCIPAL INVESTIGATOR: Wain, Harold PhD

ASSOCIATES: Sandman, Les CPT MC; Radcliffe, Elizabeth MA

DEPARTMENT: Department of Psychiatry

STATUS: Ongoing

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the relationship between hypnotic capacity, as measured by the Hypnotic Induction Profile (HIP) and dissociative experience, as measured by the Dissociative Experience Scale (DES).

TECHNICAL APPROACH

Seventy-five competent, adult psychiatric outpatients new to WRAMC's Department of Psychiatry will be given the DES questionnaire at the same time that they are asked to fill out other data to initiate their evaluation. The DES will have a cover letter asking for the patient's involvement in the study and indicating their treatment at WRAMC will not change by participation. After the patient has been seen by a psychiatrist, he will be asked to participate in the administration of the HIP.

PRIOR AND CURRENT PROGRESS

Forty-eight patients have been completed to date.

CONCLUSIONS

Preliminary results suggest a correlation between hypnosis and dissociation. Additionally, preliminary results have enhanced diagnosis and treatment strategies.

REPORT DATE: 06/13/91

WORK UNIT # 7242

DETAIL SUMMARY SHEET

TITLE: Thyroid Function Abnormalities in Psychiatric Admissions

KEYWORDS: thyroid, psychiatry, depression

PRINCIPAL INVESTIGATOR: Hough, David CPT MC

ASSOCIATES: Burman, Kenneth MD; Sokol, Michael MD

DEPARTMENT: Department of Psychiatry

STATUS: Completed
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 5,496 Previous FYs: \$ 0 Total: \$ 5,496

STUDY OBJECTIVE

To determine prospectively the incidence of thyroid function abnormalities in 40 acute psychiatric inpatient admissions and a group of 40 control patients, to compare the means of various thyroid function tests between the two groups, and to determine if there is a correlation between psychiatric diagnoses and thyroid function abnormalities.

TECHNICAL APPROACH

The thyroid functions will be studied of 40 consecutive admissions to the acute care psychiatric wards at Walter Reed Army Medical Center and of control patients from the Kyle Metabolic Unit and the Neurology Ward. The thyroid function tests used will be third generation ultra-sensitive TSH, Free T3 and T4, and Total T3 and T4 measured by RIA.

PRIOR AND CURRENT PROGRESS

The blood samples have been drawn and tested. The results are being compiled, and some statistical analysis has been done. The total number of thyroid abnormalities did not differ significantly between the two groups. There were 11/40 (27.5%) abnormalities in the psychiatric group and 8/40 (20% in the control group. The difference in the group means for T4 was 10.4 for the psychiatric patients and 8.97 for the control group. This difference was maintained over the 10- day study period. This was a highly significant ($p=.001$) result. The differences in the group means for T3 were 2.24 for the psychiatric patients and 2.11 for the control group. This difference was maintained over the 10-day period. It was a statistically significant ($p=.01$) result. Looking at the group means for TSH, the psychiatric group had a mean value which was consistently lower than that of the control group. This result was not statistically significant ($p=.08$).

CONCLUSIONS

There appears to be little difference between psychiatric and control patients in numbers of thyroid function abnormalities. There appears to be a significant elevation of the mean value of T4 and T3 in the psychiatric population and a trend towards a lower TSH. There may be an association between major affective disorders and thyroid dysfunction, as well as a higher incidence of thyroid function abnormality in female patients.

REPORT DATE: 03/28/91

WORK UNIT # 9106

DETAIL SUMMARY SHEET

TITLE: Differences in Proportions of Diagnosis Between Ethnic Groups: The Case of Puerto Rican Psychiatric Patients in the Military

KEYWORDS: Hispanic, diagnosis, Puerto Rican

PRINCIPAL INVESTIGATOR: Jones, Franklin MD

ASSOCIATES: Lozano, Mary PhD; Compton, Alan COL MC

DEPARTMENT: Department of Psychiatry

STATUS: Ongoing

APPROVAL DATE: Dec 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

1) To determine whether Hispanic and other minority patients are diagnosed and managed differently from non-minority patients at WRAMC, and 2) To determine whether certain diagnoses are made more commonly in Hispanic patients than other ethnic groups.

TECHNICAL APPROACH

Psychiatric records were reviewed for 2 years with sorting of all Hispanic surnamed patients in comparison with 100 randomly selected non-Hispanic Caucasian and 100 non-Hispanic Black patients. Demographic and symptom variables are collected and compared.

PRIOR AND CURRENT PROGRESS

All Hispanic-surnamed charts and a random selection of Caucasian and Black patients charts were reviewed for diagnosis and clinical features. Review of charts is completed, and analysis is in process.

CONCLUSIONS

Island and New York Puerto Ricans seem similar and distinct from Blacks in demographic and clinical features.

REPORT DATE: 04/12/91

WORK UNIT # 4525

DETAIL SUMMARY SHEET

TITLE: Intravenous Administration of I-131-6-B Iodomethylnorcholesterol for Adrenal Evaluation and Imaging

KEYWORDS: adrenal imaging, I-131 NP-59

PRINCIPAL INVESTIGATOR: Anderson, Jay COL MC

DEPARTMENT: Department of Radiology

STATUS: Ongoing

APPROVAL DATE: Nov 1980

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To clinically evaluate NP-59 as a diagnostic agent for the detection of cortical disorders. (This radiopharmaceutical is in the category of a Phase III IND). Although these radiopharmaceuticals have been valuable in the evaluation of patients with Cushing's syndrome, primary aldosteronism, and hypoandrogenism, radiopharmaceutical companies do not find it commercially profitable to seek an NDA.

TECHNICAL APPROACH

The technical approach is unchanged. The radiopharmaceutical is obtained from the University of Michigan from Dr. Beierwaltes. The exam is only performed on those patients for whom the primary clinical physician believes potential information could be obtained and outweighs the potential risks. (In order to offer this diagnostic modality to patients, this protocol has been submitted and approved.)

PRIOR AND CURRENT PROGRESS

This radiopharmaceutical remains a valuable diagnostic tool. During this report period, nine studies were performed, with a total of 26 patients studied to date. There were no adverse reactions, and no patient has withdrawn. All studies during this period have been clinically useful.

CONCLUSIONS

No conclusion can be made nor are any conclusions anticipated. This is a standard IND to offer a diagnostic exam for patient benefit. In addition, this study saves WRAMC money because the patient is not referred to a civilian hospital to obtain the same exam.

REPORT DATE: 04/12/91

WORK UNIT # 4527

DETAIL SUMMARY SHEET

TITLE: Technetium (Tc99m) Antimony Trisulfide Colloid - A Lymphoscintigraphic Agent

KEYWORDS: lymphoscintigraphy, antimony trisulfide, colloid

PRINCIPAL INVESTIGATOR: Anderson, Jay COL MC

DEPARTMENT: Department of Radiology

STATUS: Ongoing
APPROVAL DATE: Nov 1981

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To clinically evaluate technetium (Tc99m) antimony trisulfide colloid (a Phase III IND radiopharmaceutical) in the evaluation of lymph nodes, lymphatics, and/or bone marrow distribution. Although these agents have been valuable in the evaluation of patients, radiopharmaceutical companies do not find it commercially profitable to seek an NDA. As a result, in order to offer this diagnostic modality to the patients we serve, we must have a protocol.

TECHNICAL APPROACH

The study is unchanged. The pharmaceutical is obtained from Cadema Company and labeled with the routine technetium 99m pertechnetate within our clinic. The exam is only performed on those patients for whom the primary clinical physician believes potential clinical information for the patient may be obtained. Any side effect is recorded on data sheets which are forwarded to the primary commercial company. The patient eligibility has been expanded to include pediatric patients, and this change has been approved by the appropriate review boards.

PRIOR AND CURRENT PROGRESS

This radiopharmaceutical remains an valuable diagnostic imaging tool. One hundred twenty-seven studies (127) were performed during this reporting period, with a total of 443 studies since the protocol started in 1981. The number of studies reported to be effective during this report period was 127. No untoward effects have been observed.

CONCLUSIONS

None.

REPORT DATE: 09/22/91

WORK UNIT # 4531

DETAIL SUMMARY SHEET

TITLE: Diagnostic Imaging of Adrenal Medulla (Pheochromocytoma, Paragangliomas, and Neuroblastomas) with I-131 MIBG (Metaiodobenzylguanidine Sulfate)

KEYWORDS: pheochromocytoma, I-131 MIBG

PRINCIPAL INVESTIGATOR: Anderson, Jay COL MC

DEPARTMENT: Department of Radiology

STATUS: Ongoing
APPROVAL DATE: Sep 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the use of I-131 metaiodobenzylguanidine sulfate (I-131 MIBG) as an aid in the diagnosis, evaluation, and localization of pheochromocytomas, paragangliomas, neuroblastomas, and/or adrenal medullary hyperplasia. This radiopharmaceutical has already been proven useful in the evaluation of disease noted above. Because no commercial company pursues approval by the FDA, it remains in an IND status. To reduce cost, IND from FDA was obtained to offer scan at WRAMC.

TECHNICAL APPROACH

Since this protocol is to offer a diagnostic exam for the patient rather than to do a scientific study, no experimental design compilation of data, etc., will be done. All side effects are reported to the FDA. There is no modification to the original protocol.

PRIOR AND CURRENT PROGRESS

During the current reporting period of August 1990-91, 14 patients have had I-131 MIBG studies performed. This makes a total of 72 patients since the protocol was started in 1984. There have been no adverse reactions, and no patient has withdrawn. Of the 14 patients injected during this report period, all 14 studies were clinically useful.

CONCLUSIONS

No conclusion can be made nor are any conclusions anticipated. Again, this is a standard IND to offer a diagnostic exam for patient benefit and not for a research benefit. In addition, this saves WRAMC money because the patient is not referred to a civilian hospital to obtain the same exam.

REPORT DATE: 10/10/91

WORK UNIT # 4535

DETAIL SUMMARY SHEET

TITLE: Pharyngeal and Esophageal Manifestations of Rheumatoid Arthritis

KEYWORDS: rheumatoid arthritis, esophagus

PRINCIPAL INVESTIGATOR: Meglin, Allen CPT MC

ASSOCIATES: Dachman, Abraham MD

DEPARTMENT: Department of Radiology

STATUS: Ongoing

APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To ascertain if there is a relationship between rheumatoid arthritis and esophageal disease. Similar diseases, such as scleroderma, are believed to have esophageal disease associated with them.

TECHNICAL APPROACH

Questionnaires, brief histories, and physicals are performed to see if a patient has rheumatoid arthritis. Barium swallows are performed to see if the patient has esophageal disease. These two sets of data are then compared.

PRIOR AND CURRENT PROGRESS

Data is continuing to be accumulated, and the study is expected to be concluded within the next 6 months. An additional 10 controls and 5 subjects have been enrolled and studied.

CONCLUSIONS

Data collection is nearing completion, and the study should be concluded within the next 6 months.

REPORT DATE: 09/19/91

WORK UNIT # 4538

DETAIL SUMMARY SHEET

TITLE: Ultrasound Guided Laser Ablation of Tumors

KEYWORDS: laser, liver, ultrasound

PRINCIPAL INVESTIGATOR: Dachman, Abraham MD

DEPARTMENT: Department of Radiology

STATUS: Ongoing
APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To employ an experimental technique to treat colorectal metastases limited to the liver. This is to be considered a palliative procedure that avoids the need for surgery or general anesthesia.

TECHNICAL APPROACH

Patients with limited colorectal carcinoma metastases to the liver, and not candidates for surgery, are staged using CT and ultrasound. Under ultrasound guidance, a needle is placed into the tumor and the laser fiber is placed through the needle into the tumor. An Nd:YAG laser is used at 1 to 3 watts for about 6 minutes. Sequential placement of the laser fiber in various portions of the tumor are used to attempt to totally destroy the tumor.

PRIOR AND CURRENT PROGRESS

No progress has been made due to lack of patient referral. Three patients have been referred to the protocol, but after evaluation, they did not meet inclusion criteria. Currently, there is one patient referral under evaluation. Note that under later USUHS protocols, further laboratory work was done to investigate this technique. The lab results do not warrant any change in this clinical protocol.

CONCLUSIONS

None at this time. The study remains ongoing.

REPORT DATE: 03/26/91

WORK UNIT # 2023A

DETAIL SUMMARY SHEET

TITLE: In Vitro Determination of the Response of Skeletal Muscle to Halothane, Caffeine and Halothane Plus Caffeine

KEYWORDS: skeletal muscle, halothane/caffeine, malignant hyperthermia

PRINCIPAL INVESTIGATOR: Karan, Steven MAJ MC

ASSOCIATES: Muldoon, Sheila MD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Dec 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the effect of halothane, caffeine, and halothane plus caffeine on skeletal muscle exposed to known concentrations of these agents and electrically stimulated. These tests will form the basis of normal controls for the Malignant Hyperthermia (MH) testing Laboratory at USUHS, Department of Anesthesiology.

TECHNICAL APPROACH

A small piece of skeletal muscle is removed from the paraspinal muscles in a patient undergoing lumbar laminectomy. This muscle is suspended in a Krebs-Ringer's solution and is exposed to different concentrations of halothane, caffeine, and halothane plus caffeine. The response to electrical stimulation is noted, and the results compared to patients with the clinical diagnosis of malignant hyperthermia. The protocol was amended in FY90 to include patients undergoing knee surgery, cardiac bypass surgery, and abdominal surgery for skeletal muscle from the vastus lateralis, vastus medialis, and rectus, respectively.

PRIOR AND CURRENT PROGRESS

In conjunction with North American Malignant Hyperthermia Group standards, periodic examination of control data is necessary to maintain standards and to ensure the accuracy of diagnostic MH testing. As a result of increased diagnostic testing due to Desert Shield/Storm and investigation of animal data, no human control data was obtained in this review period. Currently, an addendum to the protocol is under preparation. No new patients will be entered into the study until the addendum is completed and approved by the Human Use Committee/Institutional Review Board. At that time, an updated consent will also be submitted for approval.

CONCLUSIONS

The examination of control data continues to be vital in both understanding MH and in evaluating susceptible patients.

REPORT DATE: 08/29/91

WORK UNIT # 2032A

DETAIL SUMMARY SHEET

TITLE: Pain Control After Thoracotomy and Its Effect on Pulmonary Function

KEYWORDS: pain, thoracotomy, pulmonary function

PRINCIPAL INVESTIGATOR: Lupkas, Raymond CPT MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare three different methods of pain control after thoracotomy and evaluate the effects on pulmonary function.

TECHNICAL APPROACH

Patients are randomized to receive epidural morphine, intercostal nerve blocks, or interpleural local anesthetic for postoperative pain control. Patients are visited daily for 3 days and asked to perform a bedside pulmonary function test and to quantitate their pain using a visual analog pain scale. The original protocol has been modified to eliminate the interpleural local anesthetic group because it was found that this group did not receive adequate pain control.

PRIOR AND CURRENT PROGRESS

The study has 21 patients enrolled in both the epidural and the intercostal nerve block/PCA groups. The last year, 15 patients were enrolled, after restarting the study when the original principal investigator was deployed to Saudi Arabia. There have been no unexpected untoward sequelae to patients undergoing the study. There have been no additional benefits to patients in the study.

CONCLUSIONS

Important findings in this study will help determine if intercostal rib blocks combined with PCA (relatively simple procedure) is as effective in pain relief following thoracotomy as an epidural with narcotics (more invasive procedure).

REPORT DATE: 07/10/91

WORK UNIT # 2033A

DETAIL SUMMARY SHEET

TITLE: Incidence of Coughing Following General Anesthesia Using Fentanyl,
Sufentanil, Afentanil, and Morphine Sulfate

KEYWORDS: coughing, narcotics

PRINCIPAL INVESTIGATOR: Biggerstaff, Michael CPT MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if one specific narcotic can suppress the cough reflex more so than others.

TECHNICAL APPROACH

Patients are randomized to receive an equipotent dose of a narcotic for general anesthesia. On emergence from general anesthesia, the number of times the patient coughs is counted.

PRIOR AND CURRENT PROGRESS

Both the Principal Investigator and his assistant were deployed to Operation Desert Shield/Storm. All data collection had been completed at that time but had not been analyzed. While the investigators were away, their offices were cleaned out and the results of the study were thrown away. As both investigators have now left military service, there will be no attempt to duplicate this work.

CONCLUSIONS

None.

REPORT DATE: 06/15/91

WORK UNIT # 2038A

DETAIL SUMMARY SHEET

TITLE: Prevention of Spinal Headaches after Incidental Dural Puncture during Epidural Catheter Placement

KEYWORDS: headaches, dural puncture, epidural catheter

PRINCIPAL INVESTIGATOR: Stamatatos, John CPT MC

ASSOCIATES: Karan, Steven MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To assess prophylactic therapy for the prevention of spinal headaches after incidental dural puncture with an epidural needle.

TECHNICAL APPROACH

Patients are assigned randomly to one of the following three groups: (1) A catheter is placed through the puncture site for the anesthetic and is removed 12 hours after the procedure. (2) A catheter is placed one interspace above the puncture site with no anesthetic administered and remains in place for 12 hours after the procedure. (3) A catheter is placed one interspace above the puncture site and remains in place for 12 hours after the procedure, and saline is injected at the end of the procedure before the catheter is removed.

PRIOR AND CURRENT PROGRESS

To date, there have been eight patients enrolled in the study with a 50% reduction of headache when threading the catheter into the subarachnoid space.

CONCLUSIONS

None yet. We are waiting to enroll more patients into the study.

REPORT DATE: 09/03/91

WORK UNIT # 2039A

DETAIL SUMMARY SHEET

TITLE: Effects of Ketamine Infusion on Somatosensory Evoked Potentials

KEYWORDS: ketamine, somatosensory, evoked potentials

PRINCIPAL INVESTIGATOR: Bettencourt, Joseph CPT MC

ASSOCIATES: Lupkas, Raymond MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the effect of ketamine infusion on the latency and amplitude of somatosensory evoked potentials.

TECHNICAL APPROACH

Healthy (ASA I and II) patients, without contraindications to the use of ketamine and scheduled for elective disk surgery, are premedicated with Versed and Robinul IM, and a baseline set of median nerve and posterior tibial nerve SSEP's are measured. Anesthesia is then induced with ketamine 1mg/kg, and an infusion at 1mg/kg/hr is started. Ten minutes later, a second set of SSEP's is measured and compared with the baseline.

PRIOR AND CURRENT PROGRESS

No new subjects have been enrolled in this study since a new Principal Investigator was named because a functional evoked potential monitor has not been available. Recommend that this study be closed at this time.

CONCLUSIONS

None.

REPORT DATE: 04/08/91

WORK UNIT # 2045A

DETAIL SUMMARY SHEET

TITLE: Multicenter Study of the Davol Intraspinal Port

KEYWORDS: epidural, narcotics, cancer pain

PRINCIPAL INVESTIGATOR: Hahn, Marc, MAJ MC

ASSOCIATES: Stamatos, John CPT MC

DEPARTMENT: Department of Surgery
SERVICE: Anesthesia-Operative Service

STATUS: Ongoing
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Epidural catheters are being used with more frequency to relieve cancer pain in the terminally ill patient. Thus, this protocol will study the placement of permanent epidural catheters with intraspinal ports for the relief of cancer pain.

TECHNICAL APPROACH

A videotape, "The Placement of Davol Permanent Epidural Catheters," has been created, which is 15 minutes long and describes the technique of placement of the catheter. FDA trials are being conducted for these intraspinal ports.

PRIOR AND CURRENT PROGRESS

Eleven ports have been placed to date. We are waiting for a modification of the port to continue this study.

CONCLUSIONS

The placement of permanent epidurals for cancer pain is becoming a standard of practice in the profession. Therefore, this device will be useful in the future for the control of cancer pain.

REPORT DATE: 04/08/91

WORK UNIT # 2047A

DETAIL SUMMARY SHEET

TITLE: Preanesthetic Management in Children: A Combination of Midazolam and Ketamine

KEYWORDS: midazolam, ketamine, pediatric

PRINCIPAL INVESTIGATOR: Stamatos, John CPT MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if a combination of midazolam and ketamine would be an effective premedication for surgery in the pediatric population.

TECHNICAL APPROACH

Children 3-6 years old undergoing elective surgery will be given an intramuscular injection of 0.15 mg/kg midazolam, 1.5 mg/kg ketamine and 10 mg/kg glycopyrrolate.

PRIOR AND CURRENT PROGRESS

Eight children were enrolled in this study. There were no adverse effects. All were sedated adequately and brought to the operating room with minimal patient aggravation.

CONCLUSIONS

The combination of midazolam and ketamine is a good surgery premedicant for the pediatric population.

REPORT DATE: 04/24/91

WORK UNIT # 2050A

DETAIL SUMMARY SHEET

TITLE: Intraoperative Use of Patient Controlled Anxiolysis

KEYWORDS: patient-controlled, analgesia, stress response

PRINCIPAL INVESTIGATOR: Hahn, Marc MAJ MC

ASSOCIATES: Furukawa, Kenneth CPT MC; Baum, Andrew PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the effect of intraoperative use of a patient-controlled analgesia device for anxiolysis, provided the patient has adequate analgesia for the operation with a subarachnoid block. Is there a difference compared to standard anesthetist-administered anxiolysis?

TECHNICAL APPROACH

All patients will be given a subarachnoid anesthetic for comparable operative procedures; inguinal herniorrhaphies or knee arthroscopies. Preoperative evaluation includes psychometric testing, blood and urine samples for fentanyl and cortisol, repetitive fine motor testing, and extensive counselling. Intraoperative evaluation includes all of the above before skin incision and at skin closure. Postoperative visits repeat the preoperative measures. Analysis of questionnaires and laboratory samples is performed at the Uniformed Services University of the Health Sciences.

PRIOR AND CURRENT PROGRESS

Twenty-two patients have been enrolled in this study; however, most have been dropped due to anesthetic provider preferences to use additional benzodiazepines. The protocol has been changed to reflect these preferences. These amendments to the protocol have been forwarded to the Department of Clinical Investigation. Since these amendments have been adopted, four patients have successfully completed the study.

CONCLUSIONS

At this point data analyses have not been performed. Differences between the two groups will be evaluated after 20 patients have completed the study.

REPORT DATE: 04/24/91

WORK UNIT # 2051A

DETAIL SUMMARY SHEET

TITLE: Perioperative Myocardial Ischemia or Infarction During and Following Noncardiac Surgery in Patients who have Undergone Previous Coronary Artery Bypass Graft or Percutaneous Transluminal Coronary Artery Surgery

KEYWORDS: myocardial ischemia, myocardial infarction, hemodynamic responses

PRINCIPAL INVESTIGATOR: Reynolds, Paul MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Anesthesia-Operative Service

APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To record and compare the hemodynamic responses and the incidence of myocardial ischemia or infarction during and following non-cardiac surgery in patients who have undergone previous PTCA with those in whom previous CABG has been performed.

TECHNICAL APPROACH

Essentially we will compare intraoperative hemodynamics as well as episodes of postoperative ischemia, as documented by Holter monitoring, EKG's recorded, and cardioenzymes drawn each postoperative day for a maximum of 3 days.

PRIOR AND CURRENT PROGRESS

Thus far, 10 patients in the CABG group and eight patients in the PTCA group have been enrolled in the study and undergone surgery. The Department of Information Management has completed an interactive computer program to assist in the compilation of data collected during this study. This program will allow for the transfer of data through ASCII files to statistical analysis and worksheet programs for future analysis. None of the patients who have been studied have experienced a perioperative myocardial infarction. No interoperative ischemia has been seen.

CONCLUSIONS

None so far.

REPORT DATE: 06/07/91

WORK UNIT # 2052A

DETAIL SUMMARY SHEET

TITLE: Preanesthetic Management in Children: A Combination of Intramuscular Midazolam and Ketamine as Compared to Each Medication Separately

KEYWORDS: preoperative, pediatric, midazolam

PRINCIPAL INVESTIGATOR: Stamatos, John CPT MC

DEPARTMENT: Department of Surgery
SERVICE: Anesthesia-Operative Service

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the optimal induction agent for children about to undergo surgery it should be easily administered, have a quick onset, provide adequate amnesia and sedation without respiratory depression or hemodynamic compromise, and be eliminated quickly. In the absence of a single agent that meets these criteria, this study will try to determine if a combination of midazolam and ketamine might more closely approximate the ideal agent.

TECHNICAL APPROACH

ASA 1 and 2 patients ages 3-6 years old will be entered into the study. Each unpremedicated child will be randomly assigned to receive 10 mcg/kg glycopyrolate and either 0.3 mg/kg midazolam (Gp 1), 0.15 mg/kg midazolam + 1.5 mg/kg ketamine (Gp 2), or 3 mg/kg ketamine (Gp 3) in a single intramuscular injection. The time from injection until the child can be easily separated from his parents will be recorded using a mask acceptance technique. Each child will be evaluated 1 day postop and 1 week postop and 1 week postop for any lasting effects.

PRIOR AND CURRENT PROGRESS

To date, 13 patients have been entered into the study. There were no differences in the age of the patients, type of operation, or length of surgery. The mean time to separation from the parents was: Gp 1 (n=5), 198 sec. (range 120-211); Gp 2 (n=4), 165 sec. (range 120-269); and Gp 3 (n=4), 528 sec. (range 240-1080). Oxygen saturation on room air remained above 95% in all children prior to going to the operating room. The operative procedures lasted from 70 to 285 minutes. All of the patients were rated as fully awake on arrival to the recovery room. No patients in the study remained in the recovery room for more than the standard period prescribed by the recovery room's procedures (1 hour). None of the patients had any nightmares or difficulty sleeping according to the patients' parents when questioned 1 day and 1 week after the surgery.

CONCLUSIONS

We found that this combination of medications had a quick onset enabling easy separation from the parents. The children were not overly sedated, and none required prolonged recovery room stays. This combination of medication is a viable option when a premedication would be beneficial for the pediatric patient.

REPORT DATE: 01/17/91

WORK UNIT # 2053A

DETAIL SUMMARY SHEET

TITLE: The Comparison of Alfentanil and Sufenta as Conscious Sedatives for Extracorporeal Shock Wave Lithotripsy

KEYWORDS: conscious sedation, ESWL, lithotripsy

PRINCIPAL INVESTIGATOR: Reynolds, Paul MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Anesthesia-Operative Service

STATUS: Completed
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To compare the use of alfentanil and sufentanil in conscious sedation for extracorporeal shock wave lithotripsy (ESWL) through the use of pain and nausea visual analogue scales.

TECHNICAL APPROACH

Visual analogue scaled pain and nausea scores taken at 30 minutes into the procedure and just after the procedure in the recovery room were compared by treatment group.

PRIOR AND CURRENT PROGRESS

Thirty patients in each group were studied. There appears to be no clinically significant difference between the treatment groups. The incidence of emesis in both groups was zero. The incidence of nausea, while higher than reported by other groups for similar patients undergoing lithotripsy, was clinically insignificant; that is, no patient required treatment for their nausea.

CONCLUSIONS

The lack of difference between the groups tested represents a modification of the present narcotic sedation used at this institution for lithotripsy. This adds to the armamentarium available to anesthesiologists for treatment of patients undergoing lithotripsy.

REPORT DATE: 05/13/91

WORK UNIT # 2502

DETAIL SUMMARY SHEET

TITLE: Improving Frequency Specificity of the Auditory Brainstem Response

KEYWORDS: non-linear, windowing function, tone burst

PRINCIPAL INVESTIGATOR: Robier, Therese MS

ASSOCIATES: Fabry, David PhD; Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if one particular non-linear windowing function will provide more repeatable brain stem responses compared to a linear function in normal hearing and high frequency hearing-impaired subjects.

TECHNICAL APPROACH

Four non-linear and one linear windowing function, as well as a click stimulus, will be used to elicit brain stem responses from 30 normal hearing and 30 hearing-impaired subjects. The resultant waveforms for each subject will be compared in terms of morphology and latency of particular identifying peaks. Each waveform will be identified by the PI as well as a clinical audiologist. The latency data will then be compared between subject groups and between groups for each of six stimulus conditions.

PRIOR AND CURRENT PROGRESS

The data collection, data analyses, and a manuscript presenting the results have been completed. The manuscript is under review for publication, and a proposal has been submitted for presentation of the results at the Annual Convention of the American Speech-Language-Hearing Association in Atlanta, Georgia, November 1991.

CONCLUSIONS

Although a significant difference re: latency data existed between subject groups for the click stimulus, as was expected, there was no significant difference between subject groups for any of the windowing functions, non-linear or linear. These results indicate that any of the windowing functions could be used with a clinical population equivalent to the subject groups used in this study for brain stem function testing.

REPORT DATE: 06/05/91

WORK UNIT # 2504

DETAIL SUMMARY SHEET

TITLE: The Effect of Speech Babble on the Speech Recognition Ability of Soldiers with H-3 Physical Profiles

KEYWORDS: hearing-impaired, speech perception, noise

PRINCIPAL INVESTIGATOR: Cord, Mary MA

ASSOCIATES: Attack, Rodney PhD; Walden, Brian PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 1,119 Previous FYs: \$ 0 Total: \$ 1,119

STUDY OBJECTIVE

To develop and standardize a measure of speech recognition ability in noise to be administered to soldiers who are being evaluated by the Military Medical Retention Boards (MMRB) for possible administrative action. Such a measure will permit more objective judgements regarding relative communication handicap.

TECHNICAL APPROACH

The study will have two stages. The first experiment is designed to determine the least favorable signal-to-noise ratio (S/N) for monosyllabic words and multi-talker noise at which normal-hearing listeners can just maintain 100% correct recognition of words. In the second experiment, the speech and noise task will be presented to a large sample of H-3 profile soldiers at that S/N to derive normative data for this task.

PRIOR AND CURRENT PROGRESS

Data collection on 15 normal-hearing subjects is complete and a S/N for experiment two has been determined. To date, data has been collected on 76 H-3 profile soldiers in the Army Audiology and Speech Center. Data is also being collected at eight other Army audiology facilities. There have been no serious or unexpected adverse reactions, and no subjects have withdrawn from the study. There has been no direct benefit to patients.

CONCLUSIONS

Data collection has not yet been completed. However, preliminary data suggests that scores vary considerably from near 100% correct to relatively poor recognition, as was hypothesized. (Scores for the 76 H-3 profile soldiers tested thus far at the Army Audiology and Speech Center range from 42% to 95% correct.)

REPORT DATE: 08/12/91

WORK UNIT # 2505

DETAIL SUMMARY SHEET

TITLE: The Use of Temporal and Spectral Cues in the Identification of Vowels
by Hearing Impaired Listeners

KEYWORDS: frequency resolution, temporal resolution, hearing-impaired

PRINCIPAL INVESTIGATOR: Summers, W. Van PhD

ASSOCIATES: Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 168 Previous FYs: \$ 0 Total: \$ 168

STUDY OBJECTIVE

To determine whether hearing-impaired listeners' deficits in frequency resolution result in alterations in their reliance on frequency versus temporal information in vowel identification.

TECHNICAL APPROACH

Frequency resolution, temporal resolution, and vowel identification data will be measured for hearing-impaired listeners, normal-hearing listeners, and normal-hearing listeners in noise. Vowel stimuli will contain both temporal and spectral cues to vowel identity. The focus of the study is on whether hearing-impaired listeners with near-normal temporal resolution and impaired frequency resolution rely more on temporal information in making vowel identification decisions than normal-hearing listeners.

PRIOR AND CURRENT PROGRESS

Data collection is nearing completion, and preliminary data analyses have been conducted. Thirty-three subjects have participated, including 14 hearing-impaired listeners and 19 normal-hearing listeners. There have been no adverse reactions from subjects, and no subject has withdrawn from the study. There is no benefit to the subjects.

CONCLUSIONS

Hearing-impaired listeners tended to rely less on format frequency information and more on vowel duration information in vowel identification compared to normal-hearing listeners. Measures of frequency resolution and temporal resolution ability were no better predictors of cue reliance than simple audiometric thresholds. The findings suggest a reorganization of the perceptual weighting of various cues to segmental identity as a response to processing impairments.

DETAIL SUMMARY SHEET

TITLE: Lip Muscle Sensorimotor Gains Associated with Orofacial Movement

KEYWORDS: reflex, speech, facial

PRINCIPAL INVESTIGATOR: McClean, Michael PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 466 Previous FYs: \$ 0 Total: \$ 466

STUDY OBJECTIVE

To determine: 1) the effects of instructional set involving speech on the excitability of lip muscle reflexes, and 2) whether intentional muscle responses are dependent on stimulus magnitude in a simple reaction time task. A related goal is also to develop a procedure for controlling for the effects of reaction time in assessing the association of stimulus magnitude and intentional responses.

TECHNICAL APPROACH

Innocuous mechanical stimuli will be applied to the lips in order to serve as a reaction time stimulus and to elicit lip muscle reflexes (15-30 ms, R1; 20-50 ms, R2). EMG recordings will be obtained from upper and lower lip muscle, and EMG levels will be calculated for individual trials over several post stimulus intervals. Stimulus delivery and EMG analysis will be carried out under automated control with a Masscomp 5500 computer. Multiple regression and covariance analysis will be used to evaluate the effects of stimulus level, prestimulus EMG, reaction time, and instruction on post stimulus EMG levels.

PRIOR AND CURRENT PROGRESS

Results of these procedures on 10 normal subjects indicate that R1 and R2 levels are positively correlated with stimulus magnitude, but stimulus magnitude had little modulating effect on intentional responses. All responses showed positive association with pre-stimulus EMG level, and instructional set had significant modulating effects on reflex responses in 9 of 10 subjects. There have been no serious or adverse reactions in any subjects. Results have shown that reaction time responses may be effectively controlled through the use of multiple regression analysis, allowing for effective evaluation of the association between stimulus level and intentional responses. The general procedure is now being further refined for application with patients having different forms of speech production disorders. These techniques are likely to be extended and applied to work with adult stutterers under approved protocol Work Unit No. 2510.

CONCLUSIONS

Results of this study support the classic notion that somatic reflex magnitude are dependent on stimulus magnitude whereas intentional responses are not. Modulation of R1 and R2 by instructional set indicates that the trigeminal sensory system is modulated or tuned prior to the onset of intentional speech responses.

DETAIL SUMMARY SHEET

TITLE: Improving the Quality of Electrolaryngeal Voice: Evaluation of a New Method for Generating the Driving Signal Based on Computer Simulation of Natural Laryngeal Vibration

KEYWORDS: voice, electrolaryngeal, computer simulator

PRINCIPAL INVESTIGATOR: Montgomery, Allen PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Oct 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if improvements in the quality of voice produced by laryngectomees using a typical electrolarynx can be obtained through activating the device with an electrical signal analogous to natural laryngeal output.

TECHNICAL APPROACH

In this study we will evaluate whether it is possible to generate on a computer a more natural-sounding signal to replace the monotonous steady-state waveforms currently available in hand-held electrolarynges. Five laryngectomees experienced in using an electrolarynx produced speech with the experimental sound source and with three commercially available electrolarynges. The speech will be recorded and judged by trained listeners to determine if the experimental system is superior.

PRIOR AND CURRENT PROGRESS

All five laryngectomees have been tested. A master tape has been prepared and is now ready for perceptual evaluation by a panel of experienced speech pathologists. There have been no serious or unexpected adverse reactions and no subject withdrew from the study. No patients benefited directly from this study.

CONCLUSIONS

Data analysis has not yet been completed. However, preliminary evaluation by three speech pathologists indicated that the experimental electrolarynx sound quality is superior to commercially available devices.

DETAIL SUMMARY SHEET

TITLE: Evaluation of a Model of Measurement Error for Retesting Speech Recognition

KEYWORDS: speech recognition, reliability, psychometric model

PRINCIPAL INVESTIGATOR: Fabry, David PhD

ASSOCIATES: Demorest, Marilyn PhD; Cord, Mary MS

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Apr 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,176 Total: \$ 1,176

STUDY OBJECTIVE

To determine the applicability of the binomial-error model when speech recognition in hearing-impaired listeners is tested repeatedly.

TECHNICAL APPROACH

Subjects are hearing impaired patients attending the Aural Rehabilitation Program at the Army Audiology and Speech Center. Each individual is presented with a 200 word list of monosyllabic words on each of two occasions separated by at least 2 days. Retest variability in scores is subjected to a theoretical psychometric model based on the binomial distribution.

PRIOR AND CURRENT PROGRESS

Data collection has been completed on all 80 subjects. There were no serious or unexpected reactions, and no subjects withdrew from the study. No subjects have benefited directly from this study. Dr. Demorest (the original investigator) has completed data analysis on test-retest data. Dr. Fabry completed data analysis to identify inter-subject word-error patterns. New word lists were subjected to clinical evaluation to determine whether these abbreviated lists were accurate predictors of full-list performance.

CONCLUSIONS

Data analysis suggests that test and retest responses from the same subject are not independent, but are correlated across test items. The abbreviated word lists that were developed are effective predictors of full-list performance when specified criteria are met. These lists are now being used by clinicians in Army Audiology clinics around the country.

REPORT DATE: 08/07/91

WORK UNIT # 2577

DETAIL SUMMARY SHEET

TITLE: The Effects of Amplification and Visual Cues on Auditory Consonant Recognition Ability

KEYWORDS: hearing aids, lipreading, consonant recognition

PRINCIPAL INVESTIGATOR: Walden, Brian PhD

ASSOCIATES: Fabry, David PhD; Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Jul 1986

FUNDING: Current FY: \$ 9,453 Previous FYs: \$ 5,849 Total: \$ 15,302

STUDY OBJECTIVE

To determine the degree of redundancy between the effects of amplification and lipreading on the auditory consonant recognition ability of patients with sensorineural hearing impairments.

TECHNICAL APPROACH

Adult subjects with bilateral sensorineural hearing impairments are administered a 200-item consonant-vowel recognition test under four test conditions: unamplified auditory, unamplified auditory plus lipreading, amplified auditory, and amplified auditory plus lipreading. In addition, responses to the Hearing Aid Performance Inventory (HAPI) are obtained from each subject 3 months following administration of the consonant recognition tests. Log-linear analyses are used to compare patterns of consonant confusion under each of the four conditions of consonant recognition.

PRIOR AND CURRENT PROGRESS

Consonant recognition data have been obtained from the entire sample of 24 hearing-impaired subjects. Log-linear analyses of the consonant-vowel recognition data have been completed for all 24 subjects.

CONCLUSIONS

There is an orderly progression among the four test conditions, from most difficult (unamplified auditory) to least difficult (amplified auditory plus lipreading). Lipreading plays a highly influential role in the auditory-visual speech recognition of persons with sensorineural hearing impairment in that consonant confusions can occur in auditory-visual speech recognition that would be unlikely occurrences if the stimuli were presented by audition only.

REPORT DATE: 08/22/91

WORK UNIT # 2588

DETAIL SUMMARY SHEET

TITLE: Hearing Loss and the Perception of Complex Sounds

KEYWORDS: resolution, harmonics, spectral

PRINCIPAL INVESTIGATOR: Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Aug 1988

FUNDING: Current FY: \$ 2,913 Previous FYs: \$ 992 Total: \$ 3,905

STUDY OBJECTIVE

This work unit is a grant proposal submitted to the National Institutes of Health to obtain funding. The goal of the grant is to determine how the impaired spectral and temporal processing accompanying sensorineural hearing loss interferes with the identification and discrimination of speech-like sounds. The proposal includes seven studies, each of which will be submitted for approval as a separate protocol.

TECHNICAL APPROACH

Each of the proposed experiments includes measurements of frequency resolution and a measure of the internal representation of harmonic complexes. Frequency resolution will be assessed using a notched-noise threshold procedure which allows the tracing of the internal auditory filter. Measures of temporal and spectral processing of harmonic complexes will be made by asking subjects to identify sounds which are constructed to have some of the acoustic characteristics of speech. Confusions among selected stimuli will indicate the degree of impairment of the internal representations of those sounds, which will then be related to the measures of frequency resolution.

PRIOR AND CURRENT PROGRESS

During the past year of work on this grant, data collection and preliminary data analysis have been completed on three experiments, and pilot work is underway on two others. A total of 58 subjects have participated in protocols associated with this grant so far. There have been no adverse reactions nor any patients withdrawn from the study. There is no direct benefit to patients.

CONCLUSIONS

Each experiment proposed in this grant will be carried out under its own work unit number. Descriptions of progress and the use of human subjects will be submitted individually for each project.

REPORT DATE: 04/08/91

WORK UNIT # 2589

DETAIL SUMMARY SHEET

TITLE: Articulatory and Laryngeal Timing in the Speech of Stutterers and Nonstutterers

KEYWORDS: stutterers, speech, timing

PRINCIPAL INVESTIGATOR: Prosek, Robert PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if timing differences exist between stutterers and nonstutterers during production of a repeated utterance.

TECHNICAL APPROACH

Timing relationships that occur in the speech of stutterers, as measured by kinematics (articulatory data), electroglottography (laryngeal data), and sound spectrography (acoustic data), will be examined. Measurements of the onsets and offsets of lip, jaw, and laryngeal activity for stutterers will determine if stutterers' fluent speech is as precisely timed as that of nonstutterers.

PRIOR AND CURRENT PROGRESS

All data has been collected from the 10 normal subjects and 10 stutterers. Data for three of the subjects has been analyzed. Data analysis continues at a slow pace due to volume of data from each subject. There have been no serious or unexpected adverse reactions, and no subject withdrew from the study. No patients benefited directly from this study.

CONCLUSIONS

Data analysis has not yet been completed. However, it is hypothesized that discoordination exists between phonation and articulation in the fluent speech of stutterers.

REPORT DATE: 04/05/91

WORK UNIT # 2590

DETAIL SUMMARY SHEET

TITLE: Modeling Impaired Frequency Resolution in Normal Ears

KEYWORDS: hearing loss, frequency resolution, auditory models

PRINCIPAL INVESTIGATOR: Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 650 Previous FYs: \$ 4,355 Total: \$ 5,005

STUDY OBJECTIVE

The purpose of this study is to determine the feasibility of using signal processing of speech-like sounds to simulate the impaired cochlear processing found in individuals with sensorineural hearing loss. Successful simulation of hearing impairment may lead subsequently to a method for compensating for these impaired processing mechanisms.

TECHNICAL APPROACH

A computer model of impaired cochlear processing is being developed with parameters based on audiological measures from individual subjects. Three subjects with hearing loss will act as "templates" for testing the model. Measurements of frequency resolution are made and entered as parameters into the model. The subjects will then identify sets of vowel-like sounds, producing confusion matrices that reflect the pattern of perceptual distortions they experience. Confusion matrices obtained from normal subjects for the stimulus set processed through the model will be compared to results from the impaired subjects to assess the accuracy of the simulation of hearing loss.

PRIOR AND CURRENT PROGRESS

An upgraded and more complete cochlear model has been installed on the laboratory computer, but it has yet to be used to its full capabilities due to a deficit in computer memory and storage. These problems are being solved this month and work will resume on the model. Initial modifications of the model have been completed to allow the reconstruction of speech stimuli with distortions to simulate auditory processing by hearing-impaired subjects, and pilot stimuli have been created. Two hearing-impaired subjects have participated to date. There have been no adverse reactions, and no subjects have been withdrawn from the study. There is no benefit to the subject beyond the monetary compensation provided for their time.

CONCLUSIONS

Hypothesized modifications of the internal representations of the speech stimuli, suggested by the graphical outputs of the earlier version of the cochlear model, indicate that overall attenuation and impaired frequency resolution, both sequelae of hearing-impairment, contribute to the distortions demonstrated by the model.

REPORT DATE: 04/25/91

WORK UNIT # 2591

DETAIL SUMMARY SHEET

TITLE: Nonlinear Cochlear Processing in Normal Hearing and Hearing Impaired Listeners

KEYWORDS: spectral contrast, phase, compressive nonlinearity

PRINCIPAL INVESTIGATOR: Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 40 Previous FYs: \$ 2,099 Total: \$ 2,139

STUDY OBJECTIVE

To demonstrate the benefit to vowel identification hypothesized to occur due to a compressive nonlinearity in normal cochlear processing, and to determine whether that benefit is preserved in patients with sensorineural hearing loss.

TECHNICAL APPROACH

An internal enhancement of spectral peaks due to cochlear processing will allow good vowel discrimination even if the actual peaks have reduced amplitude. In a three-alternative forced choice task, listeners are asked to discriminate between /u/ (duke) and /oo/ (book) with the amount of spectral peak-to-valley contrast varying from 1 to 10 dB. The stimuli are presented at either a high or low intensity, and the phase relationships among the spectral components of a sound are controlled to produce either a very peaky or a very flat waveform. A comparison of performance across the intensity and phase conditions will permit assessment of the function of the cochlear nonlinearity.

PRIOR AND CURRENT PROGRESS

Data collection is now complete on this project. Since the last progress report, 13 patients and 3 normal-hearing subjects have been enrolled. The total number of subjects enrolled in the project is 19. Statistical and other data analyses are currently underway. There have been no adverse reactions from subjects, nor has any subject withdrawn from the study. There is no benefit to the subjects.

CONCLUSIONS

Preliminary analyses indicate that the internal enhancement of spectral contrast demonstrated by normal-hearing subjects is also present in patients with sloping high-frequency hearing loss, but is reduced or absent in patients with flat losses. Signal processing to increase the spectral contrast in speech might improve speech recognition for these patients.

DETAIL SUMMARY SHEET

TITLE: Abnormal Spread of Masking and ASP Hearing Aids

KEYWORDS: hearing aids, noise reduction, masking

PRINCIPAL INVESTIGATOR: Fabry, David PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 5,988 Total: \$ 5,988

STUDY OBJECTIVE

To determine whether the benefit obtained by some hearing-impaired soldiers from commercially available "noise reduction" hearing aids is related to excessive upward spread of masking.

TECHNICAL APPROACH

The signal processing characteristics used in a commercially-available noise reduction hearing aid will be simulated in a laboratory model, via Fern digital filter. In addition, the frequency response characteristics of a conventional hearing aid will also be simulated, and masking pattern data will be collected in the presence of low-frequency noise for normal and hearing-impaired subjects under both simulated hearing aid conditions. Speech recognition data will also be collected under each condition.

PRIOR AND CURRENT PROGRESS

Data collection has been completed on all subjects (5 normal and 10 hearing-impaired persons). There have been no adverse reactions from subjects, nor has any subject withdrawn from the study. The data indicate that speech recognition scores were higher under the "noise reduction" condition than the condition simulating the conventional hearing aid. There were, however, substantial inter-subject differences, suggesting that some subjects may benefit more from signal processing strategies than others.

CONCLUSIONS

Upward spread of masking was excessive for several subjects. For some subjects the "noise reduction" condition resulted in improved speech recognition that was related in a predictable way to upward spread of masking. This is restricted to bandpass noise conditions, and improvements in speech intelligibility were no greater than those achieved by normal-hearing subjects.

DETAIL SUMMARY SHEET

TITLE: Measurement of Ear Canal Sound Pressure Levels in Infants and Young Children

KEYWORDS: hearing aids, ear canal SPL, infant

PRINCIPAL INVESTIGATOR: McNeil, Donna MA

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: May 1989

FUNDING: Current FY: \$ 2,891 Previous FYs: \$ 3,329 Total: \$ 6,220

STUDY OBJECTIVE

The purpose of this study is to develop a clinically practical procedure for predicting sound pressure levels (SPL) developed in the ear canal when hearing aids are worn by very young children. Correction factors from test cavities to real-ear measurements in infants and young children will enable hearing aid output levels to be set to a level which will provide maximum gain without overamplification which could cause additional hearing loss.

TECHNICAL APPROACH

Ten adults and 30 children will participate as subjects. Aided ear canal sound pressure levels as a function of frequency will be measured using a real-ear measurement system. Subsequently, an immittance meter will be used to measure ear canal volume with a custom earmold and hearing aid in place. Then the hearing aid and earmold will be removed and tested using a 2cc acoustic coupler that has been modified to approximate the volume that was measured in the ear canal of the subject.

PRIOR AND CURRENT PROGRESS

To date, 7 of 30 children and 8 of 10 adult subjects have been tested. Earmold impressions have been taken on the remaining 2 adults, and on 6 more of the remaining 23 children. Results to date have shown increases in SPL in the ear canal in smaller ear canals, as expected. We have encountered some equipment problems, scheduling problems, and our original principal investigator left WRAMC last year. The present principal investigator has clinical responsibilities which limit the time available to complete the project. We do hope to have all subjects tested by the end of December 1991.

CONCLUSIONS

As stated above, the data collected thus far does show the expected relation between small ear canal size and increase in SPL in the ear canal. We have not tested enough subjects, however, to develop correction factors at this point.

REPORT DATE: 08/22/91

WORK UNIT # 2596

DETAIL SUMMARY SHEET

TITLE: Extracting Stable Measures from Unstable Psychophysical Performance

KEYWORDS: psychometric function, slope, simulation

PRINCIPAL INVESTIGATOR: Leek, Marjorie PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 1,862 Previous FYs: \$ 2,449 Total: \$ 4,311

STUDY OBJECTIVE

To evaluate a new method of estimating the slope and threshold on psychometric functions underlying subject performance on audiological tests.

TECHNICAL APPROACH

An adaptive threshold tracking procedure with two interleaved tracks targeting the same performance level was developed. The variability between the two tracks may be used to calculate the slope of the underlying psychometric function. The total variability within both tracks provides an indication of the stability of threshold during the course of the measurement. The procedure was developed with computer simulations and tested with human listeners using a tone-detection-in-noise task.

PRIOR AND CURRENT PROGRESS

This experiment is completed, and a paper is in press in the Journal of the Acoustical Society of America. Sixteen subjects have completed the experimental task. There have been no adverse reactions, nor have any patients been withdrawn from the study. There is no direct benefit to patients.

CONCLUSIONS

The new method provides more accurate slope estimates than more traditional calculation methods, except when the underlying threshold is changing rapidly. This method also may be used to monitor the stability of threshold over the course of the adaptive tracks, as well as to identify performance demonstrating statistically significant changes in threshold over repeated measurements.

REPORT DATE: 04/25/91

WORK UNIT # 2598

DETAIL SUMMARY SHEET

TITLE: Frequency Resolution on Hearing Impaired and Noise Masked Normal Hearing Listeners

KEYWORDS: frequency resolution, hearing-impaired, masking

PRINCIPAL INVESTIGATOR: Leek, Marjorie PhD

ASSOCIATES: Summers, W. Van PhD

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 1,995 Previous FYs: \$ 0 Total: \$ 1,995

STUDY OBJECTIVE

To determine whether the loss in frequency resolution often experienced by hearing-impaired listeners is directly related to their reduced sensitivity, and therefore might be simulated with noise masking in normal-hearing subjects, or whether a separate auditory pathology independent of elevated thresholds coexists in these patients.

TECHNICAL APPROACH

Frequency resolution in two frequency regions will be measured in normal-hearing and hearing-impaired subjects under conditions of quiet and two broadband noise masking conditions. Characteristics of the auditory filters derived from these measurements were determined to allow a comparison of both bandwidth and asymmetry of the filters across subject groups and within subjects as their sensitivity was decreased by the broadband noise floor.

PRIOR AND CURRENT PROGRESS

Data collection is complete on this project and preliminary data analyses have been carried out. Five normal-hearing and five hearing-impaired subjects have completed the study. There have been no adverse reactions from subjects, nor has any subject withdrawn from the study. There is no benefit to the subjects.

CONCLUSIONS

For both normal and hearing-impaired listeners, bandwidth and asymmetry of the auditory filters are related to sensitivity loss at the high frequency but not at low frequencies. This suggests that poor frequency resolution is caused by the same pathology that underlies the sensitivity loss. Noise masking also may simulate a hearing loss in normal subjects by producing the poor frequency resolution demonstrated by hearing-impaired patients as well as by raising threshold.

REPORT DATE: 04/23/91

WORK UNIT # 2599

DETAIL SUMMARY SHEET

TITLE: Study of the Stability of Seizure Activity in Genetically
Epilepsy-Prone Rats

KEYWORDS: genetic epilepsy, acoustic parameters, seizure stability

PRINCIPAL INVESTIGATOR: Fabry, David PhD

ASSOCIATES: Yourick, Debra PhD

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Army Audiology and Speech Center

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To investigate the acoustic parameters necessary for inducing seizures in a strain of genetically epilepsy-prone rats (GEPR-9). Specifically, we will examine whether the parameters to induce seizures are stable over repeated exposures. This basic research will help determine whether these rats are a feasible model to study the effects of novel anticonvulsant pharmacological agents.

TECHNICAL APPROACH

Rats are exposed to an acoustic stimulus of 11-14 kHz in a chamber specially designed such that sound pressure levels are controlled while providing no restraint of the rat during the running and tonic phases of the seizure. Latency-to-seizure time (duration of sound exposure before seizure), as well as seizure duration, are recorded. Seizure duration is the time from onset of seizure to the return of the righting reflex. This procedure is repeated five times separated by 48 hour periods, on all GEPR-9's, male and female.

PRIOR AND CURRENT PROGRESS

The above study has been completed, and the results indicate that 1) seizure activity is quite stable, within animals, across repeated test sessions; and 2) substantial differences exist across animals in latency-to-seizure duration. To date and for this year, 13 male and 12 female genetically epilepsy-prone rats (GEPR-9) have been used in this study. There have been no serious or unexpected adverse reactions or findings. All GEPR-9 males and females recovered from all seizures without difficulty.

CONCLUSIONS

The rats with short latency to seizure time were more consistent across exposures than those with longer latency to seizure. Most importantly, seizure activity was stable within animals across exposures. Based on these findings, GEPR-9's are a suitable animal model for the study of idiopathic epilepsy. Novel pharmacological agents may be tested in this animal model if a pre-test auditory exposure is used as a comparative.

REPORT DATE: 05/29/91

WORK UNIT # 3001

DETAIL SUMMARY SHEET

TITLE: Incidence of EKG and Cardiac Enzyme Abnormalities as an Indicator of Ischemic Heart Injury in Vascular Patients Undergoing Surgery

KEYWORDS: ischemic heart injury, cardiac enzyme, surgery

PRINCIPAL INVESTIGATOR: Stoltzfus, Daniel MAJ MC

ASSOCIATES: Whatmore, Douglas LTC MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Critical Care Medicine Service

APPROVAL DATE: Apr 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine whether Goldman and Cooperman preoperative predictors are useful in regard to vascular patients. What is the incidence of actual ischemic heart disease in postoperative vascular patients? b) To evaluate the outcome of vascular surgery patients who sustain a suspected perioperative MI. c) To better define the detection of a perioperative MI in these patients in whom blood tests for enzymes are too sensitive or not specific enough.

TECHNICAL APPROACH

Patients were interviewed prior to surgery and received both Cooperman and Goldman preoperative evaluations. Baseline EKG, CPK, and LDH isoenzymes were drawn, as well as postoperatively and each day for 7 days postsurgery.

PRIOR AND CURRENT PROGRESS

No patients have been enrolled during this fiscal year. Approximately 51 patients have been enrolled since the study began in 1985.

CONCLUSIONS

No conclusions could be drawn from the data collected that met statistical significance.

REPORT DATE: 05/14/91

WORK UNIT # 3006

DETAIL SUMMARY SHEET

TITLE: Validation of the Accuracy and Reliability of the Present System Used
in the SICU for Culturing Intravascular Catheter Segments

KEYWORDS: validation, culturing, catheter

PRINCIPAL INVESTIGATOR: Pike, James MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Critical Care Medicine Service

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To validate the current method of collection and culture of central venous catheters; that is, to determine whether plating of the catheters at the bedside as opposed to the routine submission to the lab would increase the sensitivity of identifying various organisms.

TECHNICAL APPROACH

When a central venous catheter is due to be changed or removed (3 days - MICU, 5 days - SICU) the site will be prepared and the distal 6 cm. of the catheter will be removed using a standardized approach. The segments will be divided according to the unit from which they originated and a portion will be plated on agar at the bedside while the remaining portion will be sent to the lab for processing in a routine fashion. Culture results will then be collected and verified by the PI. Demographic data will be collected and will ultimately be entered into a dBASE programming package.

PRIOR AND CURRENT PROGRESS

This protocol was initiated in July 1990, and to date approximately 150 catheter segments have been evaluated. It is anticipated that at least 200 catheters will be needed before accurate statistics can be generated. There have been no adverse reactions noted. This protocol was approved without need of a consent form since it is a validation of an ongoing routine procedure. No patients have withdrawn from the study.

CONCLUSIONS

No conclusive statistics have been generated at this time. It is expected that we will complete the initial phase of catheter collection by September 1991.

REPORT DATE: 05/22/91

WORK UNIT # 3007

DETAIL SUMMARY SHEET

TITLE: Total Parenteral Nutrition Via Pulmonary Artery Catheter

KEYWORDS: TPN, catheter, infection

PRINCIPAL INVESTIGATOR: Yowler, Charles LTC MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Critical Care Medicine Service

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To examine the hypothesis that delivery of total parenteral nutrition (TPN) via pulmonary artery catheter does not increase the risk of catheter infections above that of other multiple lumen catheters.

TECHNICAL APPROACH

Patients with pulmonary artery catheters will have any needed TPN delivered through a dedicated catheter port. Cultures will be obtained from these catheters and compared to cultures from triple lumen catheters being used to deliver TPN. Catheter infection rates will then be compared.

PRIOR AND CURRENT PROGRESS

Thirty-one patients with a total of 61 catheter lines have been entered in the study. Our study goal was 120 catheters. The primary investigator was deployed to Operation Desert Shield/Storm for 8 months which limited data collection.

CONCLUSIONS

No conclusions can be formed until additional patients and catheters are studied.

REPORT DATE: 05/02/91

WORK UNIT # 3008

DETAIL SUMMARY SHEET

TITLE: The Use of Capnography During the Transport of Intubated Patients

KEYWORDS: capnography, transport, critically ill

PRINCIPAL INVESTIGATOR: Stoltzfus, Daniel MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Critical Care Medicine Service

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 4,608 Previous FYs: \$ 0 Total: \$ 4,608

STUDY OBJECTIVE

To evaluate the information gained from a non-invasive measure of exhaled carbon dioxide while transporting mechanically ventilated, critically ill patients. Also to evaluate if the use of this device would better ensure adequate patient ventilation.

TECHNICAL APPROACH

A baseline measure (prior to transport) of the patient's minute ventilation arterial blood gas, peak airway pressure, and exhaled carbon dioxide concentration will be compared to the values obtained following transport out of the ICU to a second location. During the transport back to the ICU, the nurse, or MD will be instructed to maintain a set number (baseline while on the ventilator) of exhaled CO₂. There has been no modification to the original protocol.

PRIOR AND CURRENT PROGRESS

Three subjects were enrolled last year, and the total remains three. The most significant impediments to progress were the lack of functioning equipment, and the deployment of the PI for Operation Desert Storm. I am currently waiting for authorization of funds from MRDC which will further rectify the equipment limitation. There have been no adverse reactions, and no patients have been withdrawn from the study. No definable benefit has been provided to the patients so far.

CONCLUSIONS

Too few patients are enrolled to make a statement regarding future research. I expect that 10-20 patients will be studied within the next 3 months.

REPORT DATE: 05/28/91

WORK UNIT # 3009

DETAIL SUMMARY SHEET

TITLE: Effect of Empiric Low Dose Amphotericin B on the Development of Disseminated Candidiasis in a Surgical Intensive Care Unit

KEYWORDS: low-dose, Amphotericin B, candidiasis

PRINCIPAL INVESTIGATOR: Geiling, James MAJ MC

ASSOCIATES: Stoltzfus, Daniel MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Critical Care Medicine Service

APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if Amphotericin B in low dose (0.3 mg/kg opposed to standard dose of 0.5-1.0 mg/kg) used empirically early in a critically ill patient's course will prevent the dissemination of Candida infections.

TECHNICAL APPROACH

The study will be prospective, randomized, and single-blinded (to the patient/family), with patients receiving low-dose Amphotericin B or nothing after obtaining informed consent. Entrance criteria include persistent evidence of sepsis for less than 96 (originally 120) hours on antibiotics, multi-organ system failure involving two organ systems with evidence of Candida at one site (originally did not require evidence of Candida), or Candida isolated from two sites. Evidence of disseminated candidiasis precludes enrollment due to the need for standard dose regimens.

PRIOR AND CURRENT PROGRESS

To date nine patients have been enrolled. Decreased SICU utilization with less severely ill patients as a result of preparations for Desert Shield/Storm have resulted in less patients being enrolled than expected. No adverse effects have occurred to any patients. No specific patient benefits other than intensified monitoring have been identified in this small study population.

CONCLUSIONS

With so few numbers, no significant results have been obtained. Resumption of normal clinical services at WRAMC is expected to result in enrollment of more eligible patients. Colocation of the MICU and SICU on Ward 45 may prompt use of medical patients as well.

REPORT DATE: 05/11/91

WORK UNIT # 2035

DETAIL SUMMARY SHEET

TITLE: Investigation of the Etiology of Postoperative Hypocalcemia after
Thyroidectomy in the Thyrotoxic Patient

KEYWORDS: surgery, thyroid, hypocalcemia

PRINCIPAL INVESTIGATOR: Azarow, Kenneth CPT MC

ASSOCIATES: Beam, Thomas LTC MC; Burman, Kenneth COL MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: General Surgery Service

APPROVAL DATE: Jan 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if the thyrotoxic individual is more susceptible to hypocalcemia following thyroid surgery than is the euthyroid patient.

TECHNICAL APPROACH

Patients are evaluated in clinic preoperatively; blood is drawn for all parameters mentioned in the study. Twenty-four hour urine is obtained. Postoperative blood draws are performed by the surgical team and handled by the Principal Investigator. Patients are followed per normal post-surgical routine by the operating surgeon.

PRIOR AND CURRENT PROGRESS

Two control patients, as previously reported. Starting July 1991, the principal investigator will be back on the General Surgery Service. It is anticipated that one or two additional co-investigators will be added in order to complete the project by Spring 1992. We anticipate the control and experimental group numbers to start increasing as of July 1991.

CONCLUSIONS

Too early to determine.

REPORT DATE: 10/07/91

WORK UNIT # 2037

DETAIL SUMMARY SHEET

TITLE: The Effect of Cyclooxygenase Inhibition on Mortality and Tumor Necrosis Factor in a Lethal Model of Septic Shock in the Rat

KEYWORDS: septic shock, cyclooxygenase inhibition, tumor necrosis factor

PRINCIPAL INVESTIGATOR: Lane, Brian CPT MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Ongoing
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,365 Total: \$ 1,365

STUDY OBJECTIVE

To examine the effect of ibuprofen, a cyclooxygenase inhibitor, on mortality and tumor necrosis factor (TNF) in a clinically relevant model of septic shock in the rat.

TECHNICAL APPROACH

Using a lethal model in the rat of septic shock, a statistically relevant number of rats will be allocated to six groups to determine the effect of ibuprofen, a cyclooxygenase inhibitor, on mortality. Levels of TNF will be assayed to examine the time course of this monokine in hypermetabolic and hypometabolic phases of septic shock to determine its role in the pathophysiology of septic shock.

PRIOR AND CURRENT PROGRESS

A rapidly fatal model of rat peritonitis was used to simulate the hypometabolic phase of septic shock. Survival data was measured in hours for animals treated with ibuprofen, both pre and post infection and then compared to data from untreated rats. Preliminary results were as follows:

Treatment	N	Survival (hrs) X + SE
SEPTIC + IBU/pre-tx	20	7.04 +/- 1.31
SEPTIC + IBU/post-tx	8	7.14 +/- 1.78
SEPTIC/untreated	20	5.94 +/- 1.16
SHAM/untreated	8	All long term survivors

CONCLUSIONS

Survival results for the above model for septic untreated animals are similar to those found by other investigators (Astiz et al, CIRC CHOCK 1986). There is a small and insignificant survival difference in the treated vs untreated groups. Further work remains to be done in the investigation of animals in the hypermetabolic phase or less fulminant model of septic shock.

REPORT DATE: 10/13/91

WORK UNIT # 2043

DETAIL SUMMARY SHEET

TITLE: Fibronectin in Chronic Wounds

KEYWORDS: fibronectin, wounds

PRINCIPAL INVESTIGATOR: Steinbaum, Sarah CPT MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Completed
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether fibronectin (FN) affects healing in wounds with total loss of skin.

TECHNICAL APPROACH

This is a double blind "cross-over" study. Patients over 18 with wounds with total skin loss for 1 month participated. The patients are randomized to two initial treatments, placebo or FN. The FN is prepared from one unit of the patient's blood. A biopsy and photo are taken at the start, day 0. At 2 weeks, a photo is taken; on day 30, a biopsy, photo and cross-over to the alternate treatment occurs. A photo is taken on day 45, and biopsy and photo on day 60.

PRIOR AND CURRENT PROGRESS

Eight patients were enrolled. There were no adverse effects. Six completed the study with one requiring permanent care, and two lapsing into deterioration after initial improvement.

CONCLUSIONS

Using surface area of wounds to measure wound response proved to be inadequate. Chronic wounds do respond to cryoprecipitates but further studies with more accurate wound healing factors should be initiated.

REPORT DATE: 05/22/91

WORK UNIT # 2044

DETAIL SUMMARY SHEET

TITLE: Inflammatory Bowel Disease in the Elderly: The WRAMC Experience

KEYWORDS: Crohn's disease, IBD, ulcerative colitis

PRINCIPAL INVESTIGATOR: Zavadsky, Karen MAJ MC

ASSOCIATES: Solla, Julio MAJ MC; Pearl, Richard LTC MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Completed
APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To investigate the population of patients greater than 60 years old, presenting to Walter Reed Army Medical Center between 1978 and 1988, with a newly-diagnosed biopsy-proven inflammatory bowel disease (IBD); i.e., ulcerative colitis or Crohn's disease. The records search may be extended to include the years 1968 to 1978.

TECHNICAL APPROACH

Review of charts with attention to: sex of patients, past medical and family history, presenting symptoms, duration of symptoms prior to diagnosis, physical examination, and clinical course including (1) results of diagnostic procedures, 2) anatomic distribution of disease, 3) medical therapy and outcome, and 4) surgical therapy and outcome, and comparison to established criteria of these variables in younger IBD patients.

PRIOR AND CURRENT PROGRESS

After reviewing approximately 110 charts for the research project, only three patients who fit the criteria for the study were found. A decision was then made to discontinue the project.

CONCLUSIONS

None.

REPORT DATE: 06/01/91

WORK UNIT # 2048

DETAIL SUMMARY SHEET

TITLE: Effect of IL-1 on Glucocorticoid Inhibition of Wound Healing

KEYWORDS: IL-1, wound healing

PRINCIPAL INVESTIGATOR: Friedland, Mark CPT MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$15,076 Previous FYs: \$ 0 Total: \$ 15,076

STUDY OBJECTIVE

To determine if administration of IL-1 reverses the delay in wound healing caused by glucocorticoids. To determine the effect of administration of vitamin A on plasma IL-1 levels.

TECHNICAL APPROACH

Wound healing will be measured in a rat model using a constant speed tensiometer in a control group and in groups given steroids, vitamin A, and IL-1. IL-1 levels will be assayed in a group given steroids and vitamin A, as well as in a group given only steroids and in a control group.

PRIOR AND CURRENT PROGRESS

Due to PI's busy work schedule, the animals to be used in this study are just being received.

CONCLUSIONS

None, so far.

REPORT DATE: 06/25/91

WORK UNIT # 2049

DETAIL SUMMARY SHEET

TITLE: Serial Measurements of Cytokines in Cardiopulmonary Bypass Patients

KEYWORDS: cytokines, cardiopulmonary bypass

PRINCIPAL INVESTIGATOR: Braxton, John CPT MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: General Surgery Service

APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 1,590 Previous FYs: \$ 0 Total: \$ 1,590

STUDY OBJECTIVE

To determine the effect of a cardiopulmonary bypass on cytokines and indicators of whole body inflammatory response.

TECHNICAL APPROACH

We will place patients on bypass and draw timed blood samples to measure indicators noted above and compare degrees of change among subgroups.

PRIOR AND CURRENT PROGRESS

Adequate numbers of patients in each of three groups were obtained and values for TNF and interleukins were obtained. Data is being analyzed.

CONCLUSIONS

There appears to be a trend toward more inflammation in patients with a longer bypass.

REPORT DATE: 09/16/91

WORK UNIT # 2054

DETAIL SUMMARY SHEET

TITLE: Duodenal Malrotation - A Subtle Rotational Defect Causing Failure to Thrive

KEYWORDS: foregut, malrotation, Failure to Thrive

PRINCIPAL INVESTIGATOR: Azarow, Kenneth CPT MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Completed
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To review three cases of duodenal malrotation which have resulted in Failure to Thrive. To demonstrate that the diagnosis of this syndrome can be made with a contrast study of the upper gastrointestinal tract.

TECHNICAL APPROACH

To review the charts of the three children with this diagnosis. To describe their presentations, diagnostic evaluations, and operative interventions.

PRIOR AND CURRENT PROGRESS

Study has been completed.

CONCLUSIONS

Isolated duodenal malrotation can be associated with Failure to Thrive. This entity can be explained in children with other rotational defects of the abdomen on the basis of the embryologic timing of foregut rotation.

REPORT DATE: 08/24/91

WORK UNIT # 2055

DETAIL SUMMARY SHEET

TITLE: Modified Nissen Fundoplication: Improved Results in High Risk Children

KEYWORDS: antireflux operation, gastroesophageal reflux

PRINCIPAL INVESTIGATOR: Robie, Daniel CPT MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Completed
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To prospectively evaluate the outcome of a new modified Nissen fundoplication. We previously identified, through a retrospective review of 234 antireflux procedures in children, a high failure rate in neurologically impaired (NI) children, with wrap herniation into the chest as the most common cause of operative failure. Our modifications are an attempt to improve results in the NI and prevent wrap herniation.

TECHNICAL APPROACH

The modifications are: (1) Deliberate repair of the crus reinforced with pledgets, (2) Recreation of the angle of HIS, and (3) Anchoring the wrap to the undersurface of the diaphragm. We otherwise performed a standard Nissen fundoplication with a 360 degree wrap.

PRIOR AND CURRENT PROGRESS

Evaluation of 29 patients has been completed, with an average postoperative follow-up in 26 of 19 months. Early postoperative complications occurred in three patients; none due to recurrent reflux. Six late deaths occurred due to neurological deterioration, pulmonary disease, and medication overdose. One wrap failed with recurrence of reflux and reoperation. This wrap had not herniated into the chest. Comparing results with our retrospective review, we noted a fourfold difference in reoperation for failed Nissen, a sevenfold difference in combined failure rate (reoperations plus aspiration induced deaths), and no wrap herniations (as compared with 18 in the retrospective study).

CONCLUSIONS

The modified Nissen fundoplication prevents wrap herniation and improves postoperative results in the high-risk neurologically impaired child.

REPORT DATE: 11/12/91

WORK UNIT # 2056

DETAIL SUMMARY SHEET

TITLE: Ramification of Surgical Diseases Among HIV Positive Patients

KEYWORDS:

PRINCIPAL INVESTIGATOR: Pearl, Richard LTC MC

DEPARTMENT: Department of Surgery
SERVICE: General Surgery Service

STATUS: Terminated
APPROVAL DATE: Aug 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This protocol has been administratively terminated.

TECHNICAL APPROACH

This protocol has been administratively terminated.

PRIOR AND CURRENT PROGRESS

This protocol has been administratively terminated.

CONCLUSIONS

This protocol has been administratively terminated.

REPORT DATE: 06/26/91

WORK UNIT # 2317

DETAIL SUMMARY SHEET

TITLE: Intraocular Irrigating Solutions: Effect on Corneal Endothelium

KEYWORDS: endothelial cells, cornea, glutathione

PRINCIPAL INVESTIGATOR: Kramer, Kenyon COL MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Ophthalmology Service

APPROVAL DATE: Apr 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the relative importance of glutathione in intraocular irrigating solutions to the corneal endothelium during cataract surgery.

TECHNICAL APPROACH

Preoperative cell size measurements and corneal thickness measurements will be made. Subjects will randomly receive intraocular irrigating solutions with glutathione or without. Similar measurements will be made postoperatively and compared.

PRIOR AND CURRENT PROGRESS

Fifty-one patients have been enrolled; 33 have yielded data for analysis. There is no statistically significant difference in cell size measurements between the two groups. Three patients from the non-glutathione group with a large cell size measurement created a trend in favor of the glutathione group. The results have been published.

CONCLUSIONS

The value of glutathione in intraocular solutions for cataract surgery remains unproven.

REPORT DATE: 04/06/91

WORK UNIT # 2318

DETAIL SUMMARY SHEET

TITLE: The Effects Upon Ocular Structures of Optical Polycarbonate and of Various Eye Protective Substances Applied to and Incorporated Within It

KEYWORDS: polycarbonate, ocular eye, intraocular

PRINCIPAL INVESTIGATOR: Wertz, Fleming COL MC

ASSOCIATES: Ward, Thomas MAJ MC

DEPARTMENT: Department of Surgery

SERVICE: Ophthalmology Service

STATUS: Ongoing

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the ocular toxicity, if any, of polycarbonate lenses and various dyes applied to or incorporated within the lenses. Polycarbonate lenses are being issued as eye protection to soldiers. It is anticipated that some of these protective lenses will shatter in combat and that fragments of the lens will be driven into the eye.

TECHNICAL APPROACH

Fragments of polycarbonate, either with or without dyes, will be placed into the center of the vitreous cavity through a 20 gauge incision through the sclera. Two controls will be used: no intraocular foreign body (negative control) and iron (positive control). Parameters that will be monitored include fundus appearance, intraocular inflammation, intraocular pressure, and ERG. Animals will be euthanized at 72 hours to 6 months and the eyes examined histopathologically.

PRIOR AND CURRENT PROGRESS

Protocol has not started. Anticipate starting in Summer of 1991.

CONCLUSIONS

No conclusions.

REPORT DATE: 04/06/91

WORK UNIT # 2319

DETAIL SUMMARY SHEET

TITLE: The Efficacy of Cyanoacrylates in the Primary Closure of Conjunctival Scleral Lacerations

KEYWORDS: cyanoacrylate, scleral, laceration

PRINCIPAL INVESTIGATOR: Wertz, Fleming COL MC

ASSOCIATES: Ward, Thomas MAJ MC

DEPARTMENT: Department of Surgery

SERVICE: Ophthalmology Service

STATUS: Ongoing

APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 3,969 Previous FYs: \$ 0 Total: \$ 3,969

STUDY OBJECTIVE

To determine whether scleral lacerations can be effectively closed using cyanoacrylate glue and to determine the ocular toxicity, if any, of the glue. Currently, scleral lacerations are sutured. This is a time-consuming procedure, and it is anticipated that in combat, O.R. time will be of short supply. If lacerations could be quickly closed with glue, it would be very useful under combat conditions.

TECHNICAL APPROACH

A 6 mm scleral laceration will be created and either left open, closed with Vicryl suture in the standard fashion, or closed via the application of cyanoacrylate glue. The animals will be followed clinically by monitoring fundus appearance, intraocular pressure, intraocular inflammation, and ERG. At 72 hours to 6 months after surgery, the animals are euthanized and the eyes are examined histopathologically.

PRIOR AND CURRENT PROGRESS

Thirty animals have been used in this year (no animals were used prior to this). Our preliminary data indicate that scleral lacerations can be effectively closed with cyanoacrylate glue, at least for the short term (weeks). No ocular toxicity has yet been apparent. No histopathologic studies have been performed.

CONCLUSIONS

Preliminary data indicates that cyanoacrylate glue may be a faster method for closing scleral lacerations and would be applicable in combat conditions.

DETAIL SUMMARY SHEET

TITLE: Mood and Behavior Changes with Topical Ophthalmic Beta-Adrenergic Blockade

KEYWORDS: B-adrenergic, blockers, glaucoma

PRINCIPAL INVESTIGATOR: Cox, Kevin CPT MC

DEPARTMENT: Department of Surgery
SERVICE: Ophthalmology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if topically administered B-adrenergic blockers have an effect on mood.

TECHNICAL APPROACH

To determine subjective mood by having patients who are being treated with a topical B-blocker (or alternative drug) fill out a periodic questionnaire (Beck Depression Inventory).

PRIOR AND CURRENT PROGRESS

The study is proceeding according to protocol, but recruitment of patients did not begin until January 1991. No conclusions can be drawn from the preliminary data. Patients are still being recruited into the study. Total enrollment to date = 20 of projected 80 participants. No adverse reactions or withdrawals from the study have occurred.

CONCLUSIONS

None.

REPORT DATE: 11/21/90

WORK UNIT # 2630

DETAIL SUMMARY SHEET

TITLE: The Concomittant Use of Azathioprine and Pretransplant Transfusions

KEYWORDS: azathioprine, pretransplant, transfusions

PRINCIPAL INVESTIGATOR: Shaver, Timothy MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Organ Transplant Service

STATUS: Ongoing
APPROVAL DATE: Nov 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 362 Total: \$ 362

STUDY OBJECTIVE

To study the effectiveness of pretransplant azathioprine (Imuran) in reducing the incidence of sensitization to pretransplant blood transfusions.

TECHNICAL APPROACH

Potential recipients will be given five pretransplant tranfusions, 2 weeks apart, of stored (2-week-old) packed blood cells. They will be given azathioprine (Imuran) lmg/kg/day (50 mg/day in children) starting 1 week prior to the first tranfusion and continuing daily for 3 months after the final transfusion. One 7cc clot tube of blood will be examined for reactivity against a panel of random T and B lymphocytes.

PRIOR AND CURRENT PROGRESS

A total of 85 subjects have been transfused, with four developing T cell antibody (4/83, or 5%). Patients were considered sensitized by transfusion if their antibody to T lymphocytes increased more than 15% over baseline. Since the beginning of the protocol, 69 transplants were performed on this group. The 1 year graft survival rate was 88%, compared to a comparable group (N = 130) that received transfusions (without Imuran) who had an 81% 1 year survival rate (p = .05 not significant). The 5 year survival rate was 69% in the Imuran group, compared to 60% for the non-Imuran group. Patient enrollment is now closed. A manuscript will be prepared and submitted for publication during the upcoming fiscal year.

CONCLUSIONS

Pre-transplant transfusions with concomitant low dose Imuran have produced a low level of sensitization without blunting the transfusion effect. Sixty-one of the 85 patients in the study have been transplanted (61 primary, 8 secondary transplants). Forty-four still have functioning kidneys (72%).

REPORT DATE: 03/20/91

WORK UNIT # 2631

DETAIL SUMMARY SHEET

TITLE: Development of an Extracorporeal Liver Support System

KEYWORDS: extracorporeal, liver failure

PRINCIPAL INVESTIGATOR: Fernandez, Carlos LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Organ Transplant Service

STATUS: Ongoing
APPROVAL DATE: Jan 1986

FUNDING: Current FY: \$ 0 Previous FYs: \$ 2,195 Total: \$ 2,195

STUDY OBJECTIVE

To test an extracorporeal liver support system (ECLS) and develop SOP's for use in future clinical trials.

TECHNICAL APPROACH

Livers are removed from +10 kg pigs. The liver will be placed in the liver cassette system. The "donated" liver will be connected to a larger 20 kg pig via vascular access for extracorporeal perfusion. The production of bile by the harvested liver will suggest that the system is functional.

PRIOR AND CURRENT PROGRESS

A manuscript has been prepared and will be submitted to Military Medicine for publication.

CONCLUSIONS

Further work and sophistication need to be performed prior to any clinical attempts.

REPORT DATE: 07/22/91

WORK UNIT # 2632

DETAIL SUMMARY SHEET

TITLE: Treatment with Liver Transplantation and Human Monoclonal Anti-Hepatitis B Virus IgG of a Hepatitis B Virus Carrier who has End Stage Chronic Active Hepatitis

KEYWORDS: antibody, monoclonal, transplantation

PRINCIPAL INVESTIGATOR: Shaver, Timothy MAJ MC
ASSOCIATES: Fernandez, Carlos MD

DEPARTMENT: Department of Surgery
SERVICE: Organ Transplant Service

STATUS: Ongoing
APPROVAL DATE: Jul 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effectiveness of a new human monoclonal antihepatitis B virus antibody in the prevention of recurrent hepatitis B infection following liver transplantation in chronic hepatitis B virus carriers with end stage chronic active hepatitis.

TECHNICAL APPROACH

Patients are initially entered into the study at the University of Pittsburgh based on the need for liver transplantation secondary to chronic active hepatitis from hepatitis B virus. Once these conditions have been satisfied, the patient is then presented with the above protocol. They are treated preoperatively with injections of the monoclonal antibody, followed by liver transplantation, and then ongoing treatment postoperatively. This postoperative treatment is continued indefinitely based on the demonstrated half-life of the antibody in each patient. Once this is determined, they are then redosed on an every 2 to 4 week basis.

PRIOR AND CURRENT PROGRESS

Since the FY 90 Annual Progress Report, no additional Walter Reed patients have been entered into this study. However, two potential candidates for this study, who are Walter Reed patients, are currently awaiting transplantation at the University of Pittsburgh. The patients entered at the University of Pittsburgh are currently undergoing monthly follow-up to determine the rate of recurrence of hepatitis B in the patient receiving liver transplantation for chronic active hepatitis secondary to the hepatitis B virus. No patients with hepatic malignancy are currently being entered into the study as was done in the initial phase. No new information has been provided from this study at present.

CONCLUSIONS

In the previous APR, it was reported that the study appeared to be showing a delay in the recurrence of hepatitis B viremia in the patients receiving this antibody, and this continues to be the case, although a few patients continue to develop antibody several months to greater than 2 years from transplantation. No firm data has been generated from this study, although an interim publication is expected within the next 18 months.

REPORT DATE: 04/09/91

WORK UNIT # 2633

DETAIL SUMMARY SHEET

TITLE: Use of Antilymphocyte Preparations in Solid Organ Transplantation

KEYWORDS: antilymphocyte, preparations, transplantation

PRINCIPAL INVESTIGATOR: Fernandez, Carlos MD

ASSOCIATES: Shaver, Timothy MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Organ Transplant Service

STATUS: Ongoing
APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the long-term benefit (1-5 years post transplantation) of antilymphocyte preparations used for induction of graft tolerance to prevent rejection episodes, or in the treatment of acute rejection episodes after renal, pancreatic or hepatic transplantation.

TECHNICAL APPROACH

Minnesota ALG (MALG) will be given daily for the first 10 postoperative days and every other day for 10 days for a total of 15 doses. This will be given to high immunologic risk patients: a) >20% PRA, b) previously transplanted patients, and c) Black recipients. It will also be given to patients with poor initial renal function; i.e., Oliguria <200 cc in the first 6 hours, patients who do not respond to IV diuretics with 100 cc/hour output, and patients whose serum creatinine does not fall >2 mg/dl in the first 24 hours post transplant.

PRIOR AND CURRENT PROGRESS

Thirteen renal transplant patients have received MALG prophylactically post transplant; 11 still have functioning allografts (85%). The 1 year actuarial graft survival rate is 84.6% in this group. This compares favorably to previous prophylactic ALG protocols at this institution: 1) 1980 - 1983, 71%, and 2) 1984-1989, 85%. The only reactions to MALG were transient (<1 day) fevers in 7 of the 13 recipients. Only one of the two graft losses was due to immunologic rejection, the other was to a candida infection around the kidney as well as a vitamin K dependent coagulation problem.

CONCLUSIONS

Prophylactic ALG therapy continues to be effective in inducing immunologic tolerance in kidney transplant recipients with minimal adverse reactions. Only 2 of the 13 recipients had rejection episodes. Although some of the patients are not one year out as yet, this rejection rate (0.15/patient) compares favorably to the previous prophylactic ALG protocols 1) 1980-1983, 1.57/patient, and 2) 1984-1989, 0.78/patient.

DETAIL SUMMARY SHEET

TITLE: Determination of Epstein-Barr Virus Replication in Lateral Tongue Epithelium of Immunosuppressed Patients

KEYWORDS: tongue epithelium, oral hairy leukoplakia, Epstein-Barr Virus

PRINCIPAL INVESTIGATOR: Shaver, Timothy MAJ MC

ASSOCIATES: Childers, Esther MAJ DC; Foss, Robert LT, DC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Organ Transplant Service

APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To ascertain the presence of Epstein-Barr Virus (EBV) replication in lateral tongue epithelium of immunosuppressed and healthy individuals in order to clarify the role of Epstein-Barr virus in the etiology of oral hairy leukoplakia (OHL). Oral hairy leukoplakia is considered prognostic of AIDS, and understanding the mechanism of EBV expression could lead to further progress in the unravelling of the complex oral clinical picture of immunosuppression.

TECHNICAL APPROACH

After a brief intraoral examination, the lateral border of the participant's tongue is gently scraped with a microdissecting stainless steel curette to obtain a sample of tongue epithelium. The sample is then fixed in a solution of glutaraldehyde in formalin, and the submitted specimens are then cut, stained, and examined under light and electron microscopy. The electron microscopic identification of intranuclear EBV replication, as indicated by viral particles in various stages of assembly, is considered a positive result. These positive samples are then tested with a DNA genome probe for EBV.

PRIOR AND CURRENT PROGRESS

Five patients have been entered into the study with four scrapings, providing adequate material for examination. Due to the current postgraduate training of one of the associate investigators responsible for the electron and light microscopic examination of the specimens, no additional patients have been entered into the study, although it is anticipated that the final group of patients will be entered after July 1991. It is anticipated that this study will be completed within the previously anticipated completion date of June 1992. There have been no serious or unexpected adverse reactions, and no patients have been withdrawn from this study.

CONCLUSIONS

The only conclusion available at present is that four of five patients entered into the study have provided adequate specimens for evaluation. No additional conclusions can be drawn from the study at present.

REPORT DATE: 08/12/91

WORK UNIT # 2401

DETAIL SUMMARY SHEET

TITLE: Evaluation of Porous Coated Total Knee and Hip Prostheses in Achieving a Stable Prosthesis Bone Interface

KEYWORDS: porous, total joint, prosthesis

PRINCIPAL INVESTIGATOR: Hopkinson, William LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Ongoing
APPROVAL DATE: Aug 1983

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

Evaluate the long-term results of the use of uncemented hip and knee replacements.

TECHNICAL APPROACH

Ongoing yearly hip and knee rating (clinical) and radiographs, which are the clinical standard with or without research.

PRIOR AND CURRENT PROGRESS

The first 100 consecutive uncemented hip replacements have been followed from 5 to 7 years. Five-year follow-up data has been recorded for the patients. Statistical analysis of the data has just been completed. With the results, a paper is now being written. After completion, the paper will be submitted to the Journal of Bone and Joint Surgery. The former principal investigator, CPT Heekin, presented this study as a finalist for the Bailey K. Ashford Award, which recognizes the outstanding research efforts of graduating residents. Follow-up of this patient group will continue with ongoing yearly hip ratings and radiographs.

CONCLUSIONS

Limp as related to operative approach which was significant at 2 years was not significant at 5 years. The investigators anticipate publication of the 5-year results in JBJS.

REPORT DATE: 04/22/91

WORK UNIT # 2404

DETAIL SUMMARY SHEET

TITLE: Characterization of the Postoperative Radionuclide Scan Patterns in Patients with Porous Coated Total Hip Protheses

KEYWORDS: total hip prostheses, porous coated, radionuclide scan

PRINCIPAL INVESTIGATOR: Hopkinson, William LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Completed
APPROVAL DATE: Oct 1984

FUNDING: Current FY: \$ 0 Previous FYs: \$ 75 Total: \$ 75

STUDY OBJECTIVE

To determine the natural history of bone scan patterns, both technetium and indium-III WBC, in patients undergoing uncemented total hip replacements.

TECHNICAL APPROACH

Thirty patients underwent bone technetium and indium-III WBC scanning 7 days, 3 months, 6 months, 12 months, and 24 months after uncemented total hip replacement. The scan, plain radiographs, and clinical ratings were compared.

PRIOR AND CURRENT PROGRESS

Patients enrolled in the study continue to return for annual follow-up. Standard follow-up procedures, including AP and lateral hip radiographs, allow correlation of previous technetium and indium-III WBC scans with clinical and radiographic results at 5 to 7 years follow-up.

CONCLUSIONS

Continued analysis may allow identification of early scintigraphic findings related to late component failure and may provide insight into physiologic bone response leading to modes of failure such as aseptic loosening and osteolysis.

REPORT DATE: 09/09/91

WORK UNIT # 2410

DETAIL SUMMARY SHEET

TITLE: The Use of Arthroscopic Abrasion Chondroplasty in the Treatment of Osteoarthritis of the Knee

KEYWORDS: arthroscopic, chondroplasty, osteoarthritis

PRINCIPAL INVESTIGATOR: Hopkinson, William LTC MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Orthopaedic Surgery Service

APPROVAL DATE: Aug 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 8,439 Total: \$ 8,439

STUDY OBJECTIVE

To evaluate the results of abrasion chondroplasty as a treatment for osteoarthritis of the knee.

TECHNICAL APPROACH

Forty patients with osteoarthritis of the knee will be randomized into two treatment groups. One group will have arthroscopy and knee debridement; the other group will have arthroscopy, knee debridement, and abrasion chondroplasty. Annual knee rating, clinical exam, and radiographs will be performed.

PRIOR AND CURRENT PROGRESS

Limited progress has been made on this protocol since the Primary Investigator was deployed to the Middle East over the last year. Efforts at enrolling patients into the study will be made for one more year.

CONCLUSIONS

None at this time.

REPORT DATE: 09/18/91

WORK UNIT # 2411

DETAIL SUMMARY SHEET

TITLE: Evaluation of Spinal Instrumentation in Posterior Spinal Fusion Using Radionuclide Imaging

KEYWORDS: spinal fusion, bone scan

PRINCIPAL INVESTIGATOR: Van Dam, Bruce LTC MC

ASSOCIATES: Polly, David MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Completed
APPROVAL DATE: Sep 1988

FUNDING: Current FY: \$ 1,206 Previous FYs: \$ 0 Total: \$ 1,206

STUDY OBJECTIVE

To study the appearance of technetium and indium bone scans postoperatively at 1 week, 6 months and 1 year, compared to preoperatively, following posterior spinal fusion with instrumentation.

TECHNICAL APPROACH

Technetium and indium bone scans are performed preoperatively and at 1 week, 6 months, and 1 year postoperatively in adults undergoing posterior spinal fusion with instrumentation.

PRIOR AND CURRENT PROGRESS

The study was completed in November 1990 with the final scans performed on the last enrolled subject.

CONCLUSIONS

Scans return to baseline levels of activity by 6 months postoperative. Posterior vs. posterolateral fusions can be discerned. A "donut sign" is typical for the ilia bone graft site.

REPORT DATE: 04/01/91

WORK UNIT # 2412

DETAIL SUMMARY SHEET

TITLE: Evaluation of the Brainstem in Idiopathic Scoliosis with Magnetic Resonance Imaging

KEYWORDS: idiopathic scoliosis, MRI, brain stem

PRINCIPAL INVESTIGATOR: Geissele, Alfred CPT MC

ASSOCIATES: Van Dam, Bruce LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Completed
APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 1,707 Total: \$ 1,707

STUDY OBJECTIVE

To evaluate the anatomy of the brain stem in patients with idiopathic scoliosis in order to determine whether an anatomic abnormality exists which may be etiologic.

TECHNICAL APPROACH

Patients from the WRAMC Scoliosis Clinic with adolescent idiopathic scoliosis were selected at random for study with brain stem MRI after informed consent was obtained. The images were evaluated in a blinded fashion by three attending radiologists along with brain stem MRI's of 11 nonscoliotic controls.

PRIOR AND CURRENT PROGRESS

A significant difference in the incidence of asymmetry of the brain stem was found in 22 subjects compared to 11 controls ($p < .05$). There were no serious or unexpected adverse effects. One subject was found to have a cisterna magna cyst, an unexpected finding.

CONCLUSIONS

The etiology of idiopathic scoliosis may be found in the asymmetry of the brain stem noted in these subjects. The question now arises whether the siblings of these individuals have asymmetry on MRI and a curve too.

REPORT DATE: 05/07/91

WORK UNIT # 2413

DETAIL SUMMARY SHEET

TITLE: Evaluation of Lumbar Paraspinal Muscle Compartment Pressures Following Posterior Spinal Fusions

KEYWORDS: compartment pressure, paraspinal muscles, posterior spinal fusion

PRINCIPAL INVESTIGATOR: Van Dam, Bruce LTC MC
ASSOCIATES: Bagg, Mark CPT MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Completed
APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 2,910 Total: \$ 2,910

STUDY OBJECTIVE

To document the presence or absence of elevated (greater than 30 mm Hg) paraspinal compartment pressures following posterior spinal fusion.

TECHNICAL APPROACH

Preoperative and postoperative paraspinal compartment pressures are measured bilaterally at the L3 level. Pressures are taken with standard monitoring equipment (Stryker Co.) using an indwelling slit catheter. The personnel to conduct the project (Dr. Bagg) personally takes the pressure measurements.

PRIOR AND CURRENT PROGRESS

Seventeen patients were enrolled in the study. The average preoperative measurement was 10.7 mm Hg. The pressure recorded postoperatively measured 17.9, 13.3, 15.3, and 15.6 mm Hg at 0, 8, 16, and 24 hours postoperatively. At 48 hours, all pressure readings had returned to normal (10.5 mm Hg). The average postoperative measurement was 18.6 mm Hg, which was statistically higher than our preoperative value ($p < 0.01$). During the study, six patients were noted to have pressure exceeding 30 mm Hg, but remained less than 40 mm Hg. All pressures returned to normal by 48 hours postoperatively. Length of the surgery was noted to be longer for this group of patients; however, the difference was not significant.

CONCLUSIONS

Since the average high pressure did not exceed the threshold on 30 mm Hg and had returned to preoperative levels by 48 hours, compartment syndrome of the paraspinal muscles does not appear to be a clinical concern on routine posterior spinal fusion.

REPORT DATE: 07/30/91

WORK UNIT # 2414

DETAIL SUMMARY SHEET

TITLE: Use of Platelet Derived Growth Factor in Sarcoma Detection

KEYWORDS: PDGF, sarcoma, tumor marker

PRINCIPAL INVESTIGATOR: Berrey, Hudson LTC MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Orthopaedic Surgery Service

APPROVAL DATE: Nov 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 196 Total: \$ 196

STUDY OBJECTIVE

To determine the specificity of platelet derived growth factor (PDGF) as a sarcoma tumor marker.

TECHNICAL APPROACH

To obtain blood specimens pre- and postoperatively from patients undergoing surgery for suspected tumors. To correlate type and amount of tumor mass to level of serum PDGF.

PRIOR AND CURRENT PROGRESS

No progress has occurred within the past year due to the PI's deployment to Southwest Asia.

CONCLUSIONS

None at the current time.

REPORT DATE: 07/30/91

WORK UNIT # 2415

DETAIL SUMMARY SHEET

TITLE: Effect of Phenol on Bone Lesions in Rabbits

KEYWORDS: phenol, bone lesions, rabbit

PRINCIPAL INVESTIGATOR: Berrey, Hudson LTC MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Orthopaedic Surgery Service

APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the effectiveness of phenol in bone lesions.

TECHNICAL APPROACH

New Zealand white rabbits will be used. A hole will be drilled into the tibia of one leg. Phenol will be instilled into the hole for varying times. Tibias will be collected at 1 weeks, 2 weeks, and 1 month for pathologic exam.

PRIOR AND CURRENT PROGRESS

No progress has occurred within the past year due to the PI's deployment to Southwest Asia.

CONCLUSIONS

None at current time.

REPORT DATE: 10/23/91

WORK UNIT # 2417

DETAIL SUMMARY SHEET

TITLE: A Prospective Study of Back Pain in Pregnancy

KEYWORDS: back pain, pregnancy

PRINCIPAL INVESTIGATOR: McHale, Kathleen MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Ongoing
APPROVAL DATE: Aug 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the natural history of back pain in pregnancy and the occurrence and amount of back pain as it relates to weight gain.

TECHNICAL APPROACH

The explanation of the study and the consent form are given to the prenatal patients at the introductory visit. The questionnaire regarding back symptoms and an orthopaedic physical exam are done along with the obstetric exam once during the first, second, and third trimesters, and then at the first post partum check. If the patient continues to have pain at the post partum exam (6 weeks post partum), then the patient continues to be seen by the Orthopaedic Surgery Service until there is some resolution.

PRIOR AND CURRENT PROGRESS

Approximately 10% of the study is complete, insofar as the number of subjects enrolled (43 patients). Staffing shortages during Operation Desert Storm greatly hampered work on this study. Enrollment continues and should improve through the next fiscal year.

CONCLUSIONS

It does not appear that weight gain has influence on back pain in pregnancy.

REPORT DATE: 04/01/91

WORK UNIT # 2418

DETAIL SUMMARY SHEET

TITLE: Clinical Investigation of the PWB Spine System

KEYWORDS: PWB spine system, spinal fusion

PRINCIPAL INVESTIGATOR: van Dam, Bruce LTC MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Orthopaedic Surgery Service

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate a new pedicle fixation device which is more flexible than previously used rigid devices. It is hypothesized that lumbar and lumbosacral fusion rates will be enhanced.

TECHNICAL APPROACH

This is a multicenter study. All patients to be enrolled are candidates for lumbar or lumbosacral fusions with pedicle. There is no change in the protocol.

PRIOR AND CURRENT PROGRESS

A total of 17 subjects were enrolled in 1990 and reflect the total for this study to date. There have been no serious or unexpected adverse problems. No patients have been withdrawn from the study.

CONCLUSIONS

No conclusions can be drawn at this time. Several subjects are still within the time frame needed to heal a spinal fusion.

REPORT DATE: 03/05/91

WORK UNIT # 2419

DETAIL SUMMARY SHEET

TITLE: The Treatment of Carpal Tunnel Syndrome with Pyridoxine

KEYWORDS: carpal tunnel, pyridoxine, vitamin B6

PRINCIPAL INVESTIGATOR: Stuart, Wayne MAJ MC

ASSOCIATES: Smith, Allan COL MC

DEPARTMENT: Department of Surgery

SERVICE: Orthopaedic Surgery Service

STATUS: Ongoing

APPROVAL DATE: Dec 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define the efficacy of pyridoxine in treatment of carpal tunnel syndrome.

TECHNICAL APPROACH

Prospective randomized study of patients with documented carpal tunnel syndrome; patients treated with conservative measures versus those treated with conservative measures plus pyridoxine.

PRIOR AND CURRENT PROGRESS

Due to a change in duty station to Ft. Meade and interruption by deployment in Operation Desert Shield, PI has been unable to initiate the protocol as submitted and approved. Completion is expected upon PI's return to his duty station. The protocol will be accomplished in conjunction with the Hand Surgery Service at WRAMC.

CONCLUSIONS

Completion expected upon return of principal investigator.

REPORT DATE: 08/19/91

WORK UNIT # 2420

DETAIL SUMMARY SHEET

TITLE: MRI Characteristics following Surgical Excision of Soft Tissue Sarcomas and Radiation Therapy in Determining Normal Postsurgical and Radiation Changes from Recurrent Disease

KEYWORDS: MRI, soft tissue sarcoma, recurrent disease

PRINCIPAL INVESTIGATOR: Berrey, Hudson LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Ongoing
APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine what the signal characteristics and differences are between post irradiation changes and recurrences in soft tissue sarcomas of the extremities.

TECHNICAL APPROACH

A retrospective review will be made of MRI patients who have undergone surgery and radiation therapy for soft tissue sarcomas of the extremities.

PRIOR AND CURRENT PROGRESS

No progress was made last year due to the Principal Investigator's participation in Desert Shield/Desert Storm.

CONCLUSIONS

None, so far.

REPORT DATE: 05/29/91

WORK UNIT # 2421

DETAIL SUMMARY SHEET

TITLE: The Effect of Methotrexate on Bone Ingrowth in a Rabbit Model

KEYWORDS: methotrexate, bone ingrowth

PRINCIPAL INVESTIGATOR: Polly, David CPT MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Ongoing
APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the effect of methotrexate on bony ingrowth into a porous-coated titanium implant.

TECHNICAL APPROACH

Procedure will be performed unilaterally on the animals.

PRIOR AND CURRENT PROGRESS

The procedure was performed on 26 animals. Several problems occurred. A problem with intraoperative fracture due to the implant being larger than ordered was corrected. The procedure was then performed unilaterally on the remaining animals. Initial histomorphometry has been done, and data analysis is currently ongoing. We expect this to be completed in the next month.

CONCLUSIONS

None yet.

REPORT DATE: 07/05/91

WORK UNIT # 2422

DETAIL SUMMARY SHEET

TITLE: A Retrospective Two Year Followup of Patients Undergoing Posterior Spinal Fusion with Steffe Plate Instrumentation

KEYWORDS: Steffee VSP, spine, fusion

PRINCIPAL INVESTIGATOR: Temple, Harry CPT MC

ASSOCIATES: Van Dam, Bruce LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Completed
APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 1,238 Previous FYs: \$ 0 Total: \$ 1,238

STUDY OBJECTIVE

To evaluate our early experience with posterior spinal fusion using the Steffee VSP system. Specifically, we looked at complications, technical problems, blood loss, subjective pain and function, and the presence or absence of radiographic fusion.

TECHNICAL APPROACH

All patients with a minimum two year follow-up were evaluated by physical examination, radiographic plain films, and multiple established functional and pain questionnaires. There was no deviation from the original protocol with respect to design.

PRIOR AND CURRENT PROGRESS

A total of 34 patients have been enrolled in this study. We were able to achieve 100% follow-up in patients who had undergone posterior spinal fusion with Steffee VSP instrumentation minimally 2 years out from surgery. All data was recorded and analyzed using standard applicable statistical tests. The complication rate after retrospective review is 27%.

CONCLUSIONS

Our conclusions were that lumbar and lumbosacral fusions supplemented with Steffee instrumentation are associated with a low pseudoarthrosis rate, especially for multilevel fusions, and acceptable morbidity overall. Although radiographic fusion is the goal of surgery, other factors are important in assessing outcome. These should be taken into consideration when reporting results and in evaluating the efficacy of one treatment compared to another.

REPORT DATE: 09/18/91

WORK UNIT # 2423

DETAIL SUMMARY SHEET

TITLE: The Effects of Blood Loss on Serum Antibiotic Levels

KEYWORDS: serum antibiotic levels, blood loss, spine surgery

PRINCIPAL INVESTIGATOR: Van Dam, Bruce LTC MC

ASSOCIATES: Polly, David MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Orthopaedic Surgery Service

STATUS: Completed
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 797 Previous FYs: \$ 0 Total: \$ 797

STUDY OBJECTIVE

To determine the effect of blood loss on serum antibiotic levels during spine surgery.

TECHNICAL APPROACH

The rate of excretion of a cephalosporin antibiotic (Ancef) will be determined preoperatively with a 1 gm test load and serial serum determinations. This is repeated during surgery.

PRIOR AND CURRENT PROGRESS

The last patient completed the study in July 1991. Data is now being analyzed.

CONCLUSIONS

None.

REPORT DATE: 08/21/91

WORK UNIT # 2501

DETAIL SUMMARY SHEET

TITLE: Tensile Strength of Wounds Closed Under Increasing Tension in the Pig Model

KEYWORDS: wound closing tension, scar tensile strength, positive relationship

PRINCIPAL INVESTIGATOR: Livermore, George CPT MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Otolaryngology-Head & Neck Surgery Svc APPROVAL DATE: Mar 1990

FUNDING: Current FY: \$ 5,874 Previous FYs: \$ 0 Total: \$ 5,874

STUDY OBJECTIVE

To assess the relationship between wound closing tension and scar tensile strength in the pig animal model. A positive relationship has previously been shown in the rat model.

TECHNICAL APPROACH

Ten Hampshire pigs will be subjected to skin excisional wounds of varying degrees. The scars will be harvested at thirty days postop and sent for analysis of tensile strength, histology, and biochemical analysis. The findings will be compared for statistically significant relationships.

PRIOR AND CURRENT PROGRESS

All animal operative procedures have been completed. Initial statistical analysis shows a significant relationship. The histologic and biochemical data is still pending.

CONCLUSIONS

Conclusions will await final analysis of all data. Preliminary data support the hypothesis that there is a significant relationship between wound closing tension and scar tensile strength in the pig model.

REPORT DATE: 08/12/91

WORK UNIT # 2503

DETAIL SUMMARY SHEET

TITLE: Salicylate Ototoxicity in Humans, A Clinical Study

KEYWORDS: salicylate, aspirin, audiometric testing

PRINCIPAL INVESTIGATOR: Brammer, Robert COL MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Otolaryngology-Head & Neck Surgery Svc APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To examine the otologic effect of salicylate (specifically aspirin) in humans with conventional and high frequency audiometry with serum salicylate level correlation.

TECHNICAL APPROACH

Subjects will be accrued and undergo audiometric testing with no salicylate on board for baseline determination. Thereafter, five varying clinical dosage levels of ASA trials, by daily ingestion for a week, will be undertaken with audiometry at the end of each week. A week of rest off ASA will be given to each volunteer participant to allow return to baseline audiometric levels. Data will be collected and correlated with serum levels of ASA taken prior to each audiometric test.

PRIOR AND CURRENT PROGRESS

To date the necessary high frequency audiometer has not been purchased via the CEEP acquisition process.

CONCLUSIONS

None to date.

REPORT DATE: 03/27/91

WORK UNIT # 2582

DETAIL SUMMARY SHEET

TITLE: The Effect of Skin Undermining and Skin Excision on the Degree of
Decreased Wound Closing Tension with SMAS Plication in Fresh Cadavers

KEYWORDS: rhytidectomy, wound healing, wound tension

PRINCIPAL INVESTIGATOR: Burgess, Lawrence MAJ MC

ASSOCIATES: Kryzer, Thomas CPT MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Otolaryngology-Head & Neck Surgery Svc APPROVAL DATE: Nov 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To define the relationship between wound closing tension and flap undermining in face lift surgery, and how SMAS suspension affects both of these characteristics.

TECHNICAL APPROACH

To take wound closing measurement for different degrees of undermining, with and without SMAS suspension sutures, utilizing fresh frozen cadavers as the model.

PRIOR AND CURRENT PROGRESS

Fresh cadaver study has been completed, with nine slides studied and submitted for statistical analysis. Submission for meeting presentation is being initiated, and paper preparation is proceeding.

CONCLUSIONS

Closing tension was significantly less with SMAS plication, both anteriorly and posteriorly, and at all three levels of skin undermining. Closing tension was related to skin flap overlap by a second order exponential curve as the best fit of the variables.

DETAIL SUMMARY SHEET

TITLE: Incidence of Maxillary Sinusitis in Nasally Intubated Patients

KEYWORDS: maxillary sinusitis, intubated

PRINCIPAL INVESTIGATOR: Callahan, Scott CPT MC

ASSOCIATES: Cukier, Andrew CPT MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Otolaryngology-Head & Neck Surgery Svc APPROVAL DATE: Mar 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the incidence of maxillary sinusitis in patients with a prolonged period of indwelling nasal tubes of varying sizes and functions.

TECHNICAL APPROACH

Patients in the ICU and on the ward with nasal endotracheal tubes and/or nasogastric tubes for greater than 3 days will be evaluated with weekly sinus x-rays, and biweekly sinus ultrasounds for evidence of maxillary sinusitis. If evidence is found, a sinus puncture will be done to determine the causative organism.

PRIOR AND CURRENT PROGRESS

An updated consent form has been completed with the appropriate principal investigator listed. The personnel to conduct the project have been changed to CPT Scot Callahan, MC, Oto-H&N Surgery Service; CPT Andrew Cukier, MC, Oto-H&N Surgery Service; MAJ John Casler, MC, Oto-H&N Surgery Service; CPT Robert Balotin, MC, Dept of Radiology; and CPT Steven Rudd, MC, Dept of Radiology. The project will be discussed with the current chief of the departments of the SICU, MICU, and Radiology. Upon review of the current literature, there have been no new studies demonstrating the incidence of maxillary sinusitis in nasally intubated patients. Data will begin to be collected September 1991.

CONCLUSIONS

None yet.

REPORT DATE: 03/18/91

WORK UNIT # 2597

DETAIL SUMMARY SHEET

TITLE: Wound Healing: Development of Tensile Strength Vs. Time for Wounds
Closed Under Tension in Rats

KEYWORDS: wound healing, tension, tensile strength

PRINCIPAL INVESTIGATOR: Pickett, Bradley CPT MC

ASSOCIATES: Burgess, Lawrence MAJ MC; Livermore, George CPT MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Otolaryngology-Head & Neck Surgery Svc APPROVAL DATE: Nov 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To demonstrate the time course of development of tensile strength in wounds closed with and without tension.

TECHNICAL APPROACH

The study will be performed by dividing Sprague-Dawley rats into experimental and control groups. In the experimental group, skin will be removed from the area of the panniculus carnosus and wounds will be closed creating approximately 90 grams of closing tension. Control rats will have transverse incisions closed under minimal tension. Rats will be sacrificed at 5, 7, 10, 14 and 21 days. The wounds will then be harvested and subjected to breakload testing.

PRIOR AND CURRENT PROGRESS

The experimental procedure has been completed and the results have been analyzed. Abstracts have been submitted, but as of this time, the study has not been selected for presentation. Formal writing of the scientific paper is currently under way. The results show a significant difference in tensile strength beginning at 7 days. Polynomial regression reveals an exponential relationship between wound tensile strength and healing time in experimental and control groups.

CONCLUSIONS

When compared to wounds closed without tension, wounds closed with tension show greater wound tensile strength beginning as early as 7 days. Also, the relationship between wound tensile strength and healing time is exponential.

REPORT DATE: 12/10/91

WORK UNIT # 2111

DETAIL SUMMARY SHEET

TITLE: Normalization of Endothelial Phenotype on Vascular Grafts

KEYWORDS: endothelial cells, hyperplasia, vascular surgery

PRINCIPAL INVESTIGATOR: Sharefkin, John MD

DEPARTMENT: Department of Surgery

STATUS: Terminated

SERVICE: Peripheral Vascular Surgery Service

APPROVAL DATE: May 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To test the hypothesis that endothelial cell derived smooth muscle mitogens play an important role in the causation of smooth muscle hyperplasia at sites of blood vessel reconstruction.

TECHNICAL APPROACH

To employ cultures of adult human saphenous vein endothelial cells and adult human smooth muscle cells to study the effects of culture substrates and growth factors on endothelial cell mitogen gene expression and paracrine stimulation of smooth muscle cell mitosis.

PRIOR AND CURRENT PROGRESS

This protocol has been administratively terminated.

CONCLUSIONS

This protocol has been administratively terminated.

REPORT DATE: 09/06/91

WORK UNIT # 2113

DETAIL SUMMARY SHEET

TITLE: Fibronectin in Stasis Ulcers

KEYWORDS: fibronectin, stasis, platelet

PRINCIPAL INVESTIGATOR: Coffey, James MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Peripheral Vascular Surgery Service

APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

This study is designed to determine if autologous fibronectin (cryoprecipitate) and platelet derived growth factor (platelets) improved healing of stasis ulcers.

TECHNICAL APPROACH

Autologous cryoprecipitate and platelets were combined and applied to the surface of stasis ulcers twice a day under semipermeable membrane dress. Autologous albumin served as a control.

PRIOR AND CURRENT PROGRESS

No patients have been entered into this study by the principal investigator.

CONCLUSIONS

While there have been reports of improved healing with cryoprecipitate, current methodology does not allow separation of factors to be sure if autologous fibronectin and platelet derived growth factor are the contributing elements.

REPORT DATE: 08/12/91

WORK UNIT # 2906

DETAIL SUMMARY SHEET

TITLE: Intracellular Studies with Epidermal Growth Factor

KEYWORDS: EGF, processing

PRINCIPAL INVESTIGATOR: Robie, Daniel MAJ MC

ASSOCIATES: Schaudies, Paul CPT MS

DEPARTMENT: Department of Surgery
SERVICE: Plastic Surgery Service

STATUS: Ongoing
APPROVAL DATE: Mar 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

a) To determine the effect of epidermal growth factor (EGF) on human breast cancer cell lines; b) To study interactions between growth factor and malignant cells; and c) To measure levels of EGF and receptors in benign and malignant breast disease.

TECHNICAL APPROACH

Attempt to establish malignant cell lines and to assay cells in terms of binding internalization, processing and growth responsiveness to EGF. Lyophilized homogenates of normal and pathologic breast tissue will be measured for content of EGF using a radioimmunoassay. Comparison between benign and malignant breast disease for EGF content and correlation with patient factors (i.e., hormone levels) will be calculated.

PRIOR AND CURRENT PROGRESS

A total of 19 specimens from 19 patients were analyzed from June to October 1989. There were five breast cancer specimens, 10 benign breast disease, and 4 normal breast tissue specimens studied. A wide variation in EGF content was found in each group, between groups, and in individual specimens tested twice. This brought into question the validity of the assay, especially specimen preparation (homogenization). Also, protein content and receptor levels were not quantified, severely limiting conclusions derived from the results.

CONCLUSIONS

No apparent difference in EGF content was noted between benign and malignant breast tissue. Variability in measured EGF/gm specimen, especially when tested twice, identified problems with the assay that compromised results. Future efforts will include concurrent receptor and protein analysis.

REPORT DATE: 05/30/91

WORK UNIT # 2909

DETAIL SUMMARY SHEET

TITLE: Analysis of Antibiotic Diffusion Rates and Bacteriocidal Efficacy of Diffused Antibiotics Across a Silicone Breast Implant

KEYWORDS: antibiotic, diffusion, implant

PRINCIPAL INVESTIGATOR: Barbar, Bryon CDR MC
ASSOCIATES: Alexander, Janette LCDR MC

DEPARTMENT: Department of Surgery
SERVICE: Plastic Surgery Service

STATUS: Ongoing
APPROVAL DATE: May 1990

FUNDING: Current FY: \$ 1,042 Previous FYs: \$ 0 Total: \$ 1,042

STUDY OBJECTIVE

To investigate the rate of gentomycin diffusion through a silicone membrane in a double lumen breast implant.

TECHNICAL APPROACH

80 milligrams of gentomycin will be diluted with 50 cc of normal saline. Fluid will then be placed in the lumen of a double saline-gel breast implant. The implant will be incubated at 37 degrees C in a beaker of saline. Samples of the saline bath surrounding the implant will be collected at various times over 2 weeks. Samples will be submitted for antibiotic concentration analysis. On the original study ANCEF was being studied but in the pilot study the concentration of ANCEF that diffused through the silicone was insufficient for analysis. The study therefore has been limited to gentomycin analysis.

PRIOR AND CURRENT PROGRESS

The study analyzing the gentomycin diffusion rate in the saline/gel implant has been completed. All assays have been done and the results show that there is a progressive increase in concentration of diffusion of the antibiotic over a 2 week period. The implants which contain the antibiotics that were placed directly on an agar plate inoculated with staph epidermidis, showed insufficient diffusion of antibiotics to inhibit growth of the bacteria in the newer style low "bleed" implant. The silicone I (the old style implant) was also tested in this study and was shown to allow sufficient diffusion to inhibit bacterial growth. This indicates that although antibiotic is diffused out in measurable rates in the newer style implant its concentration is insufficient to provide bacterial-static conditions.

CONCLUSIONS

Gentomycin diffuses in measurable quantities through a silicone II implant but does not diffuse in concentrations sufficient to create a bacteria static environment. A third type of implant to be tested (non-silicone gel implant) has not arrived from the company. They will be analyzed for gentomycin diffusion and inhibition of bacterial growth on an agar plate as were the silicone gel implants.

REPORT DATE: 06/05/91

WORK UNIT # 2710

DETAIL SUMMARY SHEET

TITLE: Fresh Tissue Procurement for NIH Tissue Culture

KEYWORDS: colon mucosa, bronchial epithelial, pleural fluids

PRINCIPAL INVESTIGATOR: Edwards, Fred LTC MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Thoracic Surgery Service

APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To study the metabolic activation and deactivation of chemical carcinogens in cultured lung and colon explants. To study the capability of human lung and colon epithelium to metabolize chemical carcinogens to mutagens. To investigate biochemical differences of normal and tumor tissue.

TECHNICAL APPROACH

Lung and colon tissue removed at time of biopsy or resection are transported to NIH where tissue cultures will be established and cytochemical studies performed. These results will be compared to demographic and environmental profiles.

PRIOR AND CURRENT PROGRESS

There have been 26 cancers and 13 lymphocyte preparations brought to the NIH during the year April 1990 to April 1991.

CONCLUSIONS

This study has been renewed by the NIH for another 4 years and will continue.

REPORT DATE: 09/24/90

WORK UNIT # 2711

DETAIL SUMMARY SHEET

TITLE: Platelet Derived Growth Factor in the Healing of Stab Wounds

KEYWORDS: PDGF, wound, healing

PRINCIPAL INVESTIGATOR: Braxton, Maceo MAJ MC

ASSOCIATES: Barry, Michael, MAJ MC; Bellamy, Ronald COL MC

DEPARTMENT: Department of Surgery
SERVICE: Thoracic Surgery Service

STATUS: Completed
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if the "stab wound" is a quantitative model of wound healing and to establish whether or not Platelet Derived Growth Factor (PDGF) improves the healing of surgical stab wounds.

TECHNICAL APPROACH

This is a randomized, single-blinded, controlled, non-placebo study of the effects of PDGF on the healing of thoracotomy tube stab wounds. Only patients who have bilateral "stab wounds" will be studied. The wounds will be made using a template; so that each could serve as its own control and that all wounds are as similar as possible. Wounds will be treated with PDGF or left untreated on a random basis.

PRIOR AND CURRENT PROGRESS

This study never came to fruition. The stab wound proved to be easily healed by purse string suture. The saphenous vein wound has a complication rate of almost 20% in some series, but even here, there is no simple way of measuring healing.

CONCLUSIONS

The rate of healing of clean surgical wounds is a methodological problem. A new proposal is under preparation to use the following technologies: rate of water vaporization from the wound, hardness of the wound, near infrared spectroscopy of the wound, qualitative and quantitative measure of the protein exudate from the wound. None of these methods will be definitive. The only unequivocal method will be large clinical trials of great size and expense.

REPORT DATE: 04/05/91

WORK UNIT # 2837

DETAIL SUMMARY SHEET

TITLE: NPCP 2200 A Comparison of Leuprolide with Leuprolide and Flutamide in Previously Untreated Patients with Clinical Stage D2 Cancer of the Prostate

KEYWORDS: leuprolide, flutamide, prostate cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1985

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To try and determine if the antiandrogen flutamide will increase the efficacy of leuprolide.

TECHNICAL APPROACH

Patients are randomized to receive leuprolide and flutamide or leuprolide and placebo. At the time of progression, the blind is broken, and patients not receiving flutamide will be given the drug.

PRIOR AND CURRENT PROGRESS

This study is a multiple group cooperative effort, and accrual of 600 patients is expected. WRAMC randomized 24 patients to the protocol. Two patients are being followed on drug. Three patients are being followed off drug. Eighteen patients have died due to prostate cancer. One patient is lost to follow-up.

CONCLUSIONS

In patients with advanced prostate cancer, treatment with both leuprolide and flutamide is superior to treatment with leuprolide alone.

REPORT DATE: 01/21/91

WORK UNIT # 2839

DETAIL SUMMARY SHEET

TITLE: UCOG 100: A Phase II Trial of Interferon Alpha 2-b (INTRON A) as Adjunct Therapy in Resected Renal Cell Carcinoma at High Risk or Relapse

KEYWORDS: interferon alpha 2-b, intron A, renal cell cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Completed
APPROVAL DATE: Feb 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of intron A when given in an adjuvant setting to patients surgically cured of renal cell carcinoma at high risk of recurrence. The effect of intron A on the frequency and sites of relapses shall be determined. Progression-free survival and overall survival will be the primary endpoints of the study.

TECHNICAL APPROACH

This is a multicenter, randomized Phase III clinical trial in which patients rendered pathologically disease-free following resection of Stage III or non-metastatic Stage IV tumor will receive either adjuvant intron A three times a week (M,W,F) for 6 months or no further treatment.

PRIOR AND CURRENT PROGRESS

This is a multicenter study, and accrual for the study is expected to total 100 patients. WRAMC has randomized eight (8) patients. Four patients were randomized to receive drug. All four patients have completed taking drug. Four patients were randomized to observation. Two of these patients have had a relapse of disease. All patients are alive. All eight patients are actively being followed in the Urology Clinic.

CONCLUSIONS

It was the intent of this study to accrue 100 patients. The accrual has been extremely slow. The Oncology Clinical Research Group of Schering-Plough has decided to terminate the study.

REPORT DATE: 04/05/91

WORK UNIT # 2843

DETAIL SUMMARY SHEET

TITLE: ECOG EST 1887 A Phase III Trial of Cystectomy Alone Vs. Neoadjuvant
M-VAC + Cystectomy in Patients with Locally Advanced Bladder Cancer

KEYWORDS: cisplatin, cystectomy, bladder cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

In patients with locally advanced bladder cancer: (1) To compare the survival of those treated with cystectomy alone to those treated with M-VAC (methotrexate/vinblastine/Adriamycin/cisplatin) followed by cystectomy in a randomized Phase III neoadjuvant trial; and (2) To quantify the "tumor downstaging" effect of neoadjuvant M-VAC.

TECHNICAL APPROACH

Randomized, multicenter, Phase III trial for patients with T2-T4a, NO, MO transitional cell carcinoma of the bladder with or without squamous differentiation. Patients are randomized to radical cystectomy or M-VAC plus radical cystectomy.

PRIOR AND CURRENT PROGRESS

One patient is enrolled in this study. The patient was randomized to M-VAC plus radical cystectomy and is doing very well with the therapy he was assigned.

CONCLUSIONS

None.

REPORT DATE: 01/21/91

WORK UNIT # 2846

DETAIL SUMMARY SHEET

TITLE: ECOG EST 4887 A Phase III Trial of Bleomycin, Etoposide and Cisplatin
Vs. Etoposide and Cisplatin without Bleomycin in Minimal Extent and
Moderate Extent (Good Prognosis) Disseminated Germ Cell Tumors

KEYWORDS: bleomycin, etoposide, cisplatin

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Completed
APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether three courses of etoposide and cisplatin (EP) is equivalent in cure rate to three courses of "standard" chemotherapy consisting of bleomycin, etoposide, and cisplatin (BEP) in testicular cancer patients with minimal or moderate disease.

TECHNICAL APPROACH

Randomized, multicenter, Phase III trial for male patients with a histologic diagnoses of germ cell tumor not curable with standard radiotherapy or retroperitoneal lymph node dissection. Patients are randomized to cisplatin-etoposide-bleomycin or cisplatin-etoposide.

PRIOR AND CURRENT PROGRESS

Six patients have been enrolled in this study from WRAMC. If the six patients enrolled, four have had to have retroperitoneal lymph node dissections.

CONCLUSIONS

None at this time.

REPORT DATE: 04/05/91

WORK UNIT # 2847

DETAIL SUMMARY SHEET

TITLE: ECOG EST 5886 A Phase III Trial of Cisplatin Alone or in Combination with Doxorubicin, Vinblastine and Methotrexate in Advanced Bladder Cancer

KEYWORDS: doxorubicin, vinblastine, methotrexate

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Urology Service

APPROVAL DATE: Oct 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if cisplatin in combination with doxorubicin, vinblastine, and methotrexate is more effective than cisplatin alone in the treatment of patients with advanced bladder cancer, in terms of objective response rate, response duration and survival.

TECHNICAL APPROACH

Randomized, multicenter, Phase III trial for patients with histologically proven advanced bladder carcinoma, not curable by surgery or radiation therapy. Patients are randomized to cisplatin alone or methotrexate, vinblastine, Adriamycin, and cisplatin.

PRIOR AND CURRENT PROGRESS

There have been no patients randomized to this protocol from WRAMC.

CONCLUSIONS

None as yet.

REPORT DATE: 04/05/91

WORK UNIT # 2850

DETAIL SUMMARY SHEET

TITLE: ECOG EST 3887 Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer with Cisplatin Plus Etoposide with Either Bleomycin or Ifosfamide

KEYWORDS: testicular cancer, VIP, BEP

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine response rate and duration of remission of BEP compared to VIP combination therapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; and to confirm the efficacy and toxicity of intravenous mesna.

TECHNICAL APPROACH

Patients are randomized to VIP (cisplatin, ifosfamide, mesna, etoposide) or BEP (cisplatin, etoposide, bleomycin). Patients are reevaluated after 4 weeks of treatment, and are observed/treated based on patient response to randomized therapy.

PRIOR AND CURRENT PROGRESS

To date, two patients have been enrolled in this study. Both have done well on their individual treatments.

CONCLUSIONS

None.

REPORT DATE: 08/12/91

WORK UNIT # 2851

DETAIL SUMMARY SHEET

TITLE: ECOG EST 5888 Phase II Protocol for Advanced Germ Cell Neoplasms
5-Azacytidine

KEYWORDS: testicular cancer, 5-azacytidine

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Completed
APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate 5-azacytidine therapy to determine drug activity and further evaluation of toxicity in patients with advanced germ cell neoplasm who are failing primary and first line "salvage" therapy.

TECHNICAL APPROACH

Patients are registered to 5-azacytidine 150 mg/m²/day for five consecutive days and are repeated every 21 days after six cycles. Patients are evaluated based on response to therapy.

PRIOR AND CURRENT PROGRESS

No patients were entered onto this study from WRAMC. This study has met its accrual goals and is terminated as of August 1991.

CONCLUSIONS

None.

REPORT DATE: 04/09/91

WORK UNIT # 2853

DETAIL SUMMARY SHEET

TITLE: Double Blind Placebo Controlled Efficacy and Safety of Ditropan Slow Released Tablets for the Treatment of Symptoms of Bladder Instability in Non-Neuropathic Patients

KEYWORDS: Ditropan, bladder instability, non-neuropathic

PRINCIPAL INVESTIGATOR: Sihelnik, Stephen MAJ MC

DEPARTMENT: Department of Surgery

STATUS: Completed

SERVICE: Urology Service

APPROVAL DATE: Dec 1988

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the efficacy of Ditropan sustained-release tablets as a drug for the treatment of the symptoms of bladder instability in non-neuropathic patients with a urological diagnosis of idiopathic bladder instability.

TECHNICAL APPROACH

This multicenter study utilizes a randomized, double-blind, placebo-controlled, flexible-dose, parallel group design to evaluate Ditropan sustained-release tablets as a drug for the treatment of symptoms of bladder instability in non-neuropathic patients.

PRIOR AND CURRENT PROGRESS

Eleven patients completed the short-term phase of this study and are continuing on long-term follow-up. Accrual is closed for the short-term phase of this study.

CONCLUSIONS

None as yet.

REPORT DATE: 04/05/91

WORK UNIT # 2854

DETAIL SUMMARY SHEET

TITLE: ECOG EST 3886 Randomized Phase III Evaluation of Hormonal Therapy Vs. Observation in Patients with Stage D1 Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prostatectomy

KEYWORDS: zoladex, orchiectomy, adenocarcinoma/prostate

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Feb 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine the time to progression and survival in patients with histologically confirmed Stage D1 prostate cancer following radical prostatectomy and pelvic lymphadenectomy treated with no immediate hormonal therapy compared to those treated immediately with hormonal therapy.

TECHNICAL APPROACH

This is a multicenter randomized Phase III trial. Patients can be randomized to hormonal therapy or observation. Those patients randomized to observation may be registered to receive hormonal therapy if their disease progresses. All patients that progress on hormonal therapy will be followed off study drug.

PRIOR AND CURRENT PROGRESS

No patients have been randomized to this study at WRAMC.

CONCLUSIONS

None as yet.

REPORT DATE: 11/16/90

WORK UNIT # 2856

DETAIL SUMMARY SHEET

TITLE: Investigation of New Penile Prosthesis (U-2)

KEYWORDS: U-2, penile, prosthesis

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Completed
APPROVAL DATE: Apr 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

(a) Verify the performance of the device and the clinical utility to the patient; (b) Judge the quality of the clinical result relative to the alternative surgical devices; and (c) Determine that there are no unanticipated adverse responses to this intervention.

TECHNICAL APPROACH

Male patients will be chosen, ages 21 and older, at the investigator's discretion and consistent with standard practice in choosing patients for prosthetic penile surgery.

PRIOR AND CURRENT PROGRESS

A total of six patients have been enrolled in this study. Of the six patients enrolled, two (2) devices had to be replaced due to malfunction of the U-2 prosthetic device. Overall, the prosthesis functioned very well. The patients will continue to be followed in the Urology Clinic. Final report was sent out May 1990.

CONCLUSIONS

None as yet.

REPORT DATE: 08/12/91

WORK UNIT # 2858

DETAIL SUMMARY SHEET

TITLE: Treatment of Benign Prostatic Enlargement Using Balloon Dilatation

KEYWORDS: BPH, BPH dilator

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Urology Service

APPROVAL DATE: Jul 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

(1) Verify the performance of the device; (2) Determine the pressures and diameter required to dilate the prostate; (3) Determine that these are not anticipated, adverse responses to this intervention; and (4) Judge the quality of the clinical result.

TECHNICAL APPROACH

Male patients will be chosen, ages 45 and older. Patients will be selected at the investigator's discretion and consistent with standard practice in evaluating patients for prostatic surgery.

PRIOR AND CURRENT PROGRESS

We have nine patients enrolled in the 40Fr BPH dilator study. Five patients are followed in the Urology Clinic. Three patients are lost to follow-up. One patient who had severe chronic obstructive pulmonary disease died from cardiopulmonary arrest. The arrest occurred 3 months after the procedure. We have one patient enrolled in the 120Fr BPH dilator study. Three months after the procedure the patient had to have a transurethral resection of the prostate (TURP).

CONCLUSIONS

None.

REPORT DATE: 09/06/91

WORK UNIT # 2859

DETAIL SUMMARY SHEET

TITLE: SWOG 8894 A Comparison of Bilateral Orchiectomy with or without
Flutamide for the Treatment of Patients with Histologically Confirmed
Stage D2 Prostate Cancer

KEYWORDS: cancer, prostate, orchiectomy

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery

STATUS: Ongoing

SERVICE: Urology Service

APPROVAL DATE: Sep 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To test the hypothesis that total androgen blockade (orchiectomy plus
flutamide) may be better than orchiectomy alone.

TECHNICAL APPROACH

This is a prospective, randomized, double-blind, placebo-controlled study.

PRIOR AND CURRENT PROGRESS

Twenty-four patients were randomized to this protocol. Six patients have died
due to prostate cancer. The remaining patients are being followed in the
Urology Clinic.

CONCLUSIONS

None.

REPORT DATE: 03/12/91

WORK UNIT # 2860

DETAIL SUMMARY SHEET

TITLE: Expression of C-ErbB-2 Oncoprotein in Prostatic Carcinoma

KEYWORDS: C-Erb-B-2, prostate, cancer

PRINCIPAL INVESTIGATOR: Moul, Judd MAJ MC

ASSOCIATES: Kuhn, Eric MAJ MC; Sesterhan, Isabel MD

DEPARTMENT: Department of Surgery

SERVICE: Urology Service

STATUS: Ongoing

APPROVAL DATE: Oct 1989

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine if the C-Erb-B-2 oncogene protein is over expressed in prostate cancer. In breast cancer, this oncogene's expression correlates to adverse prognosis, and we seek to determine if a similar association is present for prostate cancer.

TECHNICAL APPROACH

(1) Obtain paraffin archival pathologic material from prostate cancer cases.
(2) Immunohistochemistry staining for C-Erb-B-2 oncoprotein in sections from these cases. (3) Correlation of staining to clinical outcome.

PRIOR AND CURRENT PROGRESS

We have created positive controls by inserting known copies of the C-Erb-B-2 gene into NIH 3TC cells. These cells were harvested into cell clumps and paraffin-embedded. Over 100 prostate cancer cases have been collected, and the tissue from the paraffin blocks has been cut and mounted. Staining is in progress.

CONCLUSIONS

Preliminary results reveal some of the prostate cancer cases do stain positively in the C-Erb-B-2 oncogene. Further staining and analyses are ongoing to see if this staining correlates to prognosis.

REPORT DATE: 06/20/91

WORK UNIT # 2861

DETAIL SUMMARY SHEET

TITLE: ECOG P-Z887 A Phase I Study of Intravesical Tumor Necrosis Factor in the Treatment of Superficial Bladder Cancer

KEYWORDS: intravesical, tumor necrosis factor, bladder cancer

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Completed
APPROVAL DATE: Jan 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine: 1) the safety of tumor necrosis factor (TNF) instilled into the bladder as an intravesical form of therapy for superficial bladder cancer; 2) the scope and severity of toxicity of TNF in patients with bladder cancer; 3) the dose limiting toxicities (DLT) and maximum tolerated dose of TNF; and 4) any systemic effects of TNF on other organ systems and systemic pharmacokinetics.

TECHNICAL APPROACH

Three patients will be treated at each dose level (200-250 mcg). Each patient will receive 11 treatments of TNF at a single dose level. If DLT is seen in more than one patient, an additional three patients will be entered at this dose level. If a total of three of these six patients exhibit a DLT, then dose escalation will end, and all subsequent patients will be entered at this dose level.

PRIOR AND CURRENT PROGRESS

We have three patients registered to this study. The first patient received 200 mcg; the other two patients received 1000 mcg. No side effects or toxicities were evidenced with the three patients.

CONCLUSIONS

None as yet.

REPORT DATE: 06/10/91

WORK UNIT # 2862

DETAIL SUMMARY SHEET

TITLE: Flow Cytometric Proliferative Activity in Stage I Nonseminomatous Testicular Cancer

KEYWORDS: flow cytometry, testicular cancer, Stage I

PRINCIPAL INVESTIGATOR: Moul, Judd MAJ MC

ASSOCIATES: Foley, John MAJ MC; Hitchcock, Charles MAJ MC

DEPARTMENT: Department of Surgery

SERVICE: Urology Service

STATUS: Ongoing

APPROVAL DATE: Apr 1990

FUNDING: Current FY: \$ 5,109 Previous FYs: \$ 0 Total: \$ 5,109

STUDY OBJECTIVE

To determine if DNA flow cytometric proliferative index (PI) measurement helps aid more accurate staging of clinically localized testicular cancer. To determine if this flow cytometric measurement (FCM) parameter will discern who is pathologic Stage I vs. occult Stage II.

TECHNICAL APPROACH

The cohort consists of all patients treated at Walter Reed since 1980 who were clinical Stage I preoperatively and then underwent retroperitoneal lymphadenectomy for testicular cancer. From this group, two subgroups were identified: Group 1 were patients without retroperitoneal metastases who were pathologic Stage I: Group 2 were patients with occult retroperitoneal metastases discovered and, therefore, upstaged to Stage II. Paraffin archival histological material was obtained on these cases and subjected to FCM.

PRIOR AND CURRENT PROGRESS

Approximately 60 patients have been identified who fit the above noted criteria. Paraffin archival material has been obtained on approximately 50% and letters have been written to outside referral hospitals to obtain additional orchiectomy specimen blocks. Flow cytometric analysis has been performed on approximately 30 cases, and no technical problems have been evident. Project should be completed within the next 6 months.

CONCLUSIONS

None at this time.

REPORT DATE: 07/03/91

WORK UNIT # 2863

DETAIL SUMMARY SHEET

TITLE: A Dose Response Study of the Effect of Flutamide on Benign Prostatic Hypertrophy

KEYWORDS: flutamide, BPH

PRINCIPAL INVESTIGATOR: McLeod, David COL MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Jun 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To evaluate the dose response of flutamide in patients with benign prostatic hypertrophy as measured by: a) improvement in maximum urinary flow rate, b) reduction in prostate volume, c) improvement in symptom score, and d) reduction in residual urine.

TECHNICAL APPROACH

Patients with symptoms of benign prostatic hypertrophy are randomized to placebo or flutamide. Flutamide dosages: 125 mg BID, 250 mg BID, 250 mg TID, or 250 mg QD. All drugs are given over a 24 week time span. The endpoints of the study are: urinary flow rates, prostate size, residual volume, PSA, and subjective symptoms.

PRIOR AND CURRENT PROGRESS

Five patients have entered this protocol. One patient has completed the study. Four patients are continuing to be studied. There have been no adverse reactions, side effects, or toxicities that have been severe or unexpected. All the patients are alive and well.

CONCLUSIONS

None as yet.

DETAIL SUMMARY SHEET

TITLE: ECOG EST 9887 A Phase III Trial of Treatment of Pathologic Stage C Carcinoma of the Prostate with Adjuvant Radiotherapy

KEYWORDS: prostate cancer, pathologic Stage C, adjuvant radiotherapy

PRINCIPAL INVESTIGATOR: Moul, Judd MAJ MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 500 Previous FYs: \$ 0 Total: \$ 500

STUDY OBJECTIVE

To compare in a randomized study, the disease-free survival rates in completely resected patients with pathologic Stage C (T3NOMO) carcinoma of the prostate assigned to be treated with adjuvant external beam radiotherapy to that in patients assigned to receive no adjuvant therapy. To assess the qualitative and quantitative toxicities of patients with pathologic Stage C carcinoma of the prostate when treated with external beam radiotherapy.

TECHNICAL APPROACH

After prostatectomy with pelvic lymphadenectomy and no evidence of regional lymph node or metastatic disease, the patient is randomized to receive adjuvant radiation therapy or no adjuvant therapy. All patients are off treatment 1 year after randomization or at disease progression.

PRIOR AND CURRENT PROGRESS

We have one patient enrolled in this study. He was randomized to no adjuvant therapy. The patient's PSA is less than 0.1, which is well within normal limits. Patient's performance status is 0, which is excellent.

CONCLUSIONS

None.

REPORT DATE: 08/01/91

WORK UNIT # 2865

DETAIL SUMMARY SHEET

TITLE: A Randomized Trial of Transurethral Resection of the Prostate Vs. Open Prostatectomy or Nonoperative Treatment

KEYWORDS: prostate, TURP, BTOPS

PRINCIPAL INVESTIGATOR: Sihelnik, Stephen LTC MC

DEPARTMENT: Department of Surgery
SERVICE: Urology Service

STATUS: Ongoing
APPROVAL DATE: Jul 1990

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether long-term mortality rates vary in men treated for symptomatic benign prostatic hypertrophy (BPH) by non-operative strategies vs operative means; to establish efficacy of non-operative treatment strategies vs TURP for men with symptomatic BPH; and to compare short- and long-term outcomes of TURP vs open prostatectomy for men with symptomatic BPH and large prostate glands.

TECHNICAL APPROACH

This is a multicenter clinical trial randomizing patients on a stratified basis (prostate size, anti-hypertensive, prostate anatomy) to receive either open prostatectomy, transurethral prostatectomy, or non-operative strategies (balloon dilation, alpha blockers, or watchful waiting control arm). Patients are evaluated with an initial symptom score and objective flow parameters and are followed periodically for procedure efficacy and overall mortality.

PRIOR AND CURRENT PROGRESS

Recruitment of eligible patients began October 1990. To date, the population enrolled into the study at this clinical site totals 26 subjects: 16 randomized and 10 non-randomized. Current status is as follows: 24 active participants; 1 deceased (non-study related), and 1 moved from area. There have been no serious or unexpected adverse reactions during this period. Benefits to study subjects are pending completion of the research protocol.

CONCLUSIONS

No conclusions to date. Data collection is ongoing.

REPORT DATE: 03/07/91

WORK UNIT # 9801

DETAIL SUMMARY SHEET

TITLE: Production of Positive and Negative Control Slides and Mouse Brain
Suspension for Fluorescent Rabies Antibody Test

KEYWORDS: rabies

PRINCIPAL INVESTIGATOR: Mouer, Thomas DAC
ASSOCIATES: Choyce, Richard DAC

SERVICE: Veterinary Service

STATUS: Ongoing
APPROVAL DATE: Dec 1986

FUNDING: Current FY: \$ 232 Previous FYs: \$ 66 Total: \$ 298

STUDY OBJECTIVE

To produce positive and negative control slides and absorbing suspensions for specific rabies antigen identification.

TECHNICAL APPROACH

Brain suspensions of normal and rabies infected mouse brain will be used to identify rabies antigen in suspect brain tissue. Fluorescein labelled anti-rabies globulin will be used for all positive, negative, and suspect tissue.

PRIOR AND CURRENT PROGRESS

1990

Total FA Tests Performed	122
Negative Tests	120
Positive Tests	2

CONCLUSIONS

There are no changes in this protocol.

REPORT DATE: 05/31/91

WORK UNIT # 9900

DETAIL SUMMARY SHEET

TITLE: Advanced Liquid Diet Evaluation

KEYWORDS: advanced, liquid, diet

PRINCIPAL INVESTIGATOR: Rowbothom, Linda CPT SP

ASSOCIATES: Coffey, Lauri MAJ SP

SERVICE: Womack Army Community Hospital, Fort Bragg, NC STATUS: Completed
APPROVAL DATE: Apr 1987

FUNDING: Current FY: \$ 0 Previous FYs: \$ 0 Total: \$ 0

STUDY OBJECTIVE

To determine whether commercially produced dental liquid products are acceptable to patients on a dental liquid diet following jaw injuries or other dental problems.

TECHNICAL APPROACH

Patients will be asked to rate first the current hospital dental liquid diet and then the research diet using a 7-point hedonic scale. Dietitians will also answer questionnaires on the research product. During the evaluation periods, self reporting and dietitian evaluation of portion consumed will be recorded. A repeated measure design will be used.

PRIOR AND CURRENT PROGRESS

A total of 96 patients participated in this tri-service multicenter study. No adverse reactions were reported. The mean caloric intake for the male patients was 3163 kcal and 124 grams of protein per day. Women consumed a mean intake of 1635 kcal and 62 grams of protein per day. No direct benefits were recognized from participating in this study.

CONCLUSIONS

Dieticians indicated a clear preference for the new liquid products in comparison to the current products. Nutrient and caloric intake were sufficient for male patients, but certain vitamin and mineral intakes were low for females. Since most patients were unable to consume the volumes required, it may be beneficial to reduce the portion sizes while maintaining the diet's caloric and nutrient content.